

10/798117

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PASSWORD:

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* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page for STN Seminar Schedule - N. America
NEWS 2 OCT 02 CA/CAPLUS enhanced with pre-1907 records from Chemisches
Zentralblatt
NEWS 3 OCT 19 BEILSTEIN updated with new compounds
NEWS 4 NOV 15 Derwent Indian patent publication number format enhanced
NEWS 5 NOV 19 WPIX enhanced with XML display format
NEWS 6 NOV 30 ICSD reloaded with enhancements
NEWS 7 DEC 04 LINPADOCDB now available on STN
NEWS 8 DEC 14 BEILSTEIN pricing structure to change
NEWS 9 DEC 17 USPATOLD added to additional database clusters
NEWS 10 DEC 17 IMSDRUGCONF removed from database clusters and STN
NEWS 11 DEC 17 DGENE now includes more than 10 million sequences
NEWS 12 DEC 17 TOXCENTER enhanced with 2008 MeSH vocabulary in
MEDLINE segment
NEWS 13 DEC 17 MEDLINE and LMEDELINE updated with 2008 MeSH vocabulary
NEWS 14 DEC 17 CA/CAPLUS enhanced with new custom IPC display formats
NEWS 15 DEC 17 STN Viewer enhanced with full-text patent content
from USPATOLD
NEWS 16 JAN 02 STN pricing information for 2008 now available
NEWS 17 JAN 16 CAS patent coverage enhanced to include exemplified
prophetic substances
NEWS 18 JAN 28 USPATFULL, USPAT2, and USPATOLD enhanced with new
custom IPC display formats
NEWS 19 JAN 28 MARPAT searching enhanced
NEWS 20 JAN 28 USGENE now provides USPTO sequence data within 3 days
of publication
NEWS 21 JAN 28 TOXCENTER enhanced with reloaded MEDLINE segment
NEWS 22 JAN 28 MEDLINE and LMEDELINE reloaded with enhancements
NEWS 23 FEB 08 STN Express, Version 8.3, now available
NEWS 24 FEB 20 PCI now available as a replacement to DPCI
NEWS 25 FEB 25 IFIREF reloaded with enhancements
NEWS 26 FEB 25 IMSPRODUCT reloaded with enhancements
NEWS 27 FEB 29 WPINDEX/WPIDS/WPIX enhanced with ECLA and current
U.S. National Patent Classification

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items

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NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * STN Columbus * * * * *

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=> file reg		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

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STRUCTURE FILE UPDATES: 2 MAR 2008 HIGHEST RN 1006303-40-7
 DICTIONARY FILE UPDATES: 2 MAR 2008 HIGHEST RN 1006303-40-7

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TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stdoc/properties.html>

=> s montlukast/cn
 L1 0 MONTLUKAST/CN

=> s montelukast/cn
 L2 1 MONTELUKAST/CN

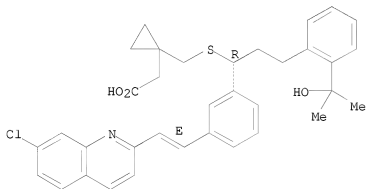
=> d l2

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2008 ACS on STN
 RN 158966-92-8 REGISTRY
 ED Entered STN: 15 Nov 1994
 CN Cyclopropaneacetic acid, 1-[[[(1R)-1-[3-[(1E)-2-(7-chloro-2-

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quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio
methyl]- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cyclopropaneacetic acid, 1-[[[1-[3-[2-(7-chloro-2-
quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio
methyl]-, [R-(E)]-
OTHER NAMES:
CN 1-[[[1-(R)-1-[3-[(E)-2-(7-Chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-
hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]cyclopropaneacetic acid
CN 2-[[[1-[(1R)-1-[3-[(1E)-2-(7-Chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-
hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]cyclopropyl]acetic acid
CN **Montelukast**
FS STEREOSEARCH
MF C35 H36 Cl N O3 S
CI COM
SR World Health Organization (WHO)
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO, CA,
CAPLUS, CASREACT, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, IMSCOSEARCH,
IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*,
PATDPASPC, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN,
USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
603 REFERENCES IN FILE CAPLUS (1907 TO DATE)

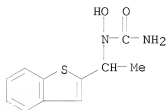
=> s zileuton/cn
L3 1 ZILEUTON/CN

=> d 13

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L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2008 ACS on STN
RN 111406-87-2 REGISTRY
ED Entered STN: 21 Nov 1987
CN Urea, N-(1-benzo[b]thien-2-ylethyl)-N-hydroxy- (CA INDEX NAME)
OTHER NAMES:
CN A 64077
CN Abbott 64077
CN Leutrol
CN N-(1-Benzo[b]thien-2-ylethyl)-N-hydroxyurea
CN **Zileuton**
CN Zyflo
DR 133305-01-8, 154003-29-9
MF C11 H12 N2 O2 S
CI COM
SR US Adopted Names Council (USAN)
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSChem, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)



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396 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
396 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s zafirlukast/cn
L4 1 ZAFIRLUKAST/CN

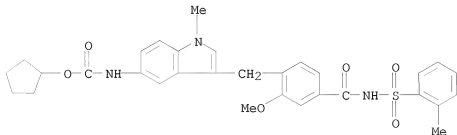
=> d 14

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2008 ACS on STN
RN 107753-78-6 REGISTRY
ED Entered STN: 26 Apr 1987
CN Carbamic acid, N-[3-[[2-methoxy-4-[[[(2-methylphenyl)sulfonyl]amino]carbonyl]phenyl]methyl]-1-methyl-1H-indol-5-yl]-, cyclopentyl ester (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Carbamic acid, [3-[[2-methoxy-4-[[[(2-methylphenyl)sulfonyl]amino]carbonyl]phenyl]methyl]-1-methyl-1H-indol-5-yl]-, cyclopentyl ester (9CI)
OTHER NAMES:
CN Accolate

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CN Cyclopentyl 3-[2-methoxy-4-[(o-tolylsulfonyl)carbonyl]benzyl]-1-methylindole-5-carbamate
CN ICI 204219
CN Vanticon
CN **Zafirlukast**
MF C31 H33 N3 O6 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

390 REFERENCES IN FILE CA (1907 TO DATE)
9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
391 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s ?lukast
LEFT TRUNCATION IGNORED FOR FILE 'REGISTRY'
L5 4 LUKAST
Left truncation is not valid in the specified search field in the specified file. The term has been searched without left truncation. Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID' would be searched as 'FLAVONOID.'

If you are searching in a field that uses implied proximity, and you used a truncation symbol after a punctuation mark, the system may interpret the truncation symbol as being at the beginning of a term. Implied proximity is used in search fields indexed as single words, for example, the Basic Index.

=> d l5 1-4

L5 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2008 ACS on STN
RN 385390-37-4 REGISTRY

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ED Entered STN: 22 Jan 2002
CN Benzenepropanoic acid, β -[(2-carboxyethyl)thio]- α -hydroxy-2-(8-phenyloctyl)-, (α S, β R)-, compd. with 1,2-ethanediamine (1:1) (9CI) (CA INDEX NAME)

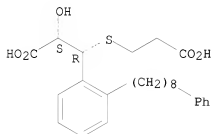
OTHER NAMES:

CN **Pobilukast edamine**
FS STEREOSEARCH
MF C26 H34 O5 S . C2 H8 N2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

CM 1

CRN 107023-41-6
CMF C26 H34 O5 S

Absolute stereochemistry. Rotation (-).



CM 2

CRN 107-15-3
CMF C2 H8 N2

H2N-CH2-CH2-NH2

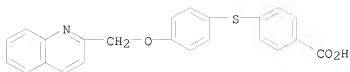
3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2008 ACS on STN
RN 252972-08-0 REGISTRY
ED Entered STN: 18 Jan 2000
CN Benzoic acid, 4-[[4-(2-quinolinylmethoxy)phenyl]thio]- (CA INDEX NAME)

OTHER NAMES:

CN **Quinlukast**
CN VUFB 19363
MF C23 H17 N O3 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ANABSTR, CA, CAPLUS, CASREACT, CHEMCATS, PROUSDDR, SYNTHLINE, TOXCENTER, USPATFULL

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

13 REFERENCES IN FILE CA (1907 TO DATE)
13 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2008 ACS on STN

RN 137232-03-2 REGISTRY

ED Entered STN: 08 Nov 1991

CN Benzenepropanoic acid, β -[(2-carboxyethyl)thio]- α -hydroxy-2-(8-phenyloctyl)-, [R-(R*,S*)]-, compd. with 1,2-ethanediamine (1:1), monohydrate (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1,2-Ethanediamine, mono[[R-(R*,S*)]- β -[(2-carboxyethyl)thio]- α -hydroxy-2-(8-phenyloctyl)benzenepropanoate], monohydrate (9CI)

OTHER NAMES:

CN (2S,3R)-3-[(2-Carboxyethyl)thio]-3-[o-(8-phenyloctyl)phenyl]lactic acid, compound with ethylenediamine (1:1), monohydrate

CN **Pobilukast edamine hydrate**

FS STEREOSEARCH

MF C26 H34 O5 S . C2 H8 N2 . H2 O

SR US Adopted Names Council (USAN)

LC STN Files: ADISINSIGHT, IMSPATENTS, IMSRESEARCH, PROUSDDR, SYNTHLINE, USAN

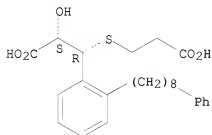
Other Sources: WHO

CM 1

CRN 107023-41-6

CMF C26 H34 O5 S

Absolute stereochemistry. Rotation (-).



CM 2

CRN 107-15-3

CMF C2 H8 N2

10/798117

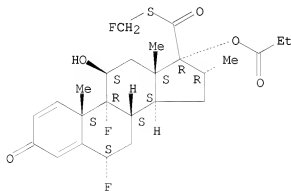
RN 80474-14-2 REGISTRY
ED Entered STN: 16 Nov 1984
CN Androsta-1,4-diene-17-carbothioic acid, 6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-, S-(fluoromethyl) ester,
(6 α ,11 β ,16 α ,17 α)- (CA INDEX NAME)

OTHER NAMES:

CN Atemur Mite
CN CCI 18781
CN Cutivate
CN Cutivate cream
CN Cyclesonide
CN Flixonase
CN Flixonase Nasal Spray
CN Flixotide
CN Flixotide Disk
CN Flixotide Disks
CN Flixotide Inhaler
CN Flonase
CN Flonase Aq
CN Flovent
CN Flovent Diskus
CN Flunase
CN Fluticasone 17-propionate
CN **Fluticasone propionate**
CN Flutide
CN Flutide N
CN Flutivate
CN Zoflut
FS STEREOSEARCH
MF C25 H31 F3 O5 S
CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, PATDPASPC, PHAR, PIRA, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



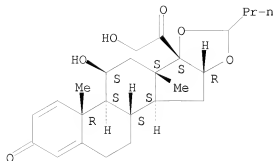
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```
=> s budesonide/cn
L9          1 BUDESONIDE/CN

=> d l9

L9  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2008 ACS on STN
RN  51333-22-3  REGISTRY
ED  Entered STN:  16 Nov 1984
CN  Pregna-1,4-diene-3,20-dione, 16,17-[butylidenebis(oxy)]-11,21-dihydroxy-,
    (11 $\beta$ ,16 $\alpha$ )- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN  2H-Naphth[2',1':4,5]indeno[1,2-d][1,3]dioxole, preгна-1,4-diene-3,20-dione
    deriv.
OTHER NAMES:
CN  16 $\alpha$ ,17 $\alpha$ -(Butylidenedioxy)-11 $\beta$ ,21-dihydroxypregna-1,4-
    diene-3,20-dione
CN  Bidien
CN  Budenofalk
CN  Budeson
CN  Budesonide
CN  Cortivent
CN  Entocort
CN  Micronyl
CN  Nebuampul
CN  Preferid
CN  Pulmicort
CN  Respules
CN  Rhinocort
CN  Rhinocort Aqua
CN  S 1320
CN  Spirocort
CN  Turbuhaler
FS  STEREOSEARCH
MF  C25 H34 O6
CI  COM
LC  STN Files:  ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS,
    BIOTECHNO, CA, CAPLUS, CASREACT, CBNE, CHEMCATS, CHEMLIST, CIN, CSCHEM,
    CSNB, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSCSEARCH,
    IMSDRUGNEWS, IMSPATENTIS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*,
    PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH, SPECINFO,
    SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
    (*File contains numerically searchable property data)
    Other Sources:  EINECS**, WHO
    (**Enter CHEMLIST File for up-to-date regulatory information)
```

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2201 REFERENCES IN FILE CA (1907 TO DATE)
 30 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 2215 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s azelastine/cn
 L10 1 AZELASTINE/CN

=> d l10

L10 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2008 ACS on STN
 RN 58581-89-8 REGISTRY
 ED Entered STN: 16 Nov 1984
 CN 1(2H)-Phthalazinone, 4-[(4-chlorophenyl)methyl]-2-(hexahydro-1-methyl-1H-azepin-4-yl)- (CA INDEX NAME)

OTHER NAMES:

CN (±)-Azelastine

CN **Azelastine**

DR 153483-42-2

MF C22 H24 Cl N3 O

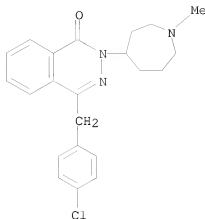
CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNE, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*, PAIDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

(*File contains numerically searchable property data)

Other Sources: WHO

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

523 REFERENCES IN FILE CA (1907 TO DATE)
10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
525 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s cetirizine/cn
L11 1 CETIRIZINE/CN

=> s fexofenadine
L12 6 FEXOFENADINE

=> s loratadine
L13 2 LORATADINE

=> s desloratadine
L14 2 DESLORATADINE

=> file medicine

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SINCE FILE	TOTAL
ENTRY	SESSION
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FULL ESTIMATED COST

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=> d his

(FILE 'HOME' ENTERED AT 08:55:09 ON 03 MAR 2008)

FILE 'REGISTRY' ENTERED AT 08:55:39 ON 03 MAR 2008

L1	0 S MONTLUKAST/CN
L2	1 S MONTELUKAST/CN
L3	1 S ZILEUTON/CN
L4	1 S ZAFIRLUKAST/CN
L5	4 S ?LUKAST
L6	1 S FLUTICASONE PROPIONATE/CN

10/798117

L7 0 S MOMETASONE FUORATE MONOHYDRATE/CN
L8 1 S MOMETASONE/CN
L9 1 S BUDESONIDE/CN
L10 1 S AZELASTINE/CN
L11 1 S CETIRIZINE/CN
L12 6 S FEXOFENADINE
L13 2 S LORATADINE
L14 2 S DESLORATADINE

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CAPLUS, DDFB, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ESBIODBASE, IFIPAT, IMSDRUGNEWS, IMSPRODUCT, IPA, KOSMET, LIFESCI, MEDLINE, NAPRALERT, NLDB, NUTRACEUT, PASCAL, PCTGEN, PHARMAML, ...' ENTERED AT 09:06:08 ON 03 MAR 2008

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17 FILES SEARCHED...
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L15 11824 L2 OR L3 OR L4 OR L5

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23 FILES SEARCHED...
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L16 32489 L6 OR L8 OR L9

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14 FILES SEARCHED...
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32 FILES SEARCHED...
'L17' IS NOT A VALID FIELD CODE
L17      32316 L10 OR L11 OR L12 OR L13 OR L14

=> s c reactive protein or inflammation
8 FILES SEARCHED...
33 FILES SEARCHED...
L18      2287254 C REACTIVE PROTEIN OR INFLAMMATION

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=> s l15 and l16 and l17

L19 420 L15 AND L16 AND L17

=> s l18 and l19

L20 128 L18 AND L19

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=> dup rem
ENTER L# LIST OR (END):120
DUPLICATE IS NOT AVAILABLE IN 'ADISINSIGHT, ADISNEWS, DGENE, DRUGMONOG2,
IMPRODUCT, KOSMET, NUTRACEUT, PCTGEN, PHARMAML, USGENE'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L20
L21      100 DUP REM L20 (28 DUPLICATES REMOVED)

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=> d l21 91-100 ibib, kwic

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L21 ANSWER 91 OF 100 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights
reserved on STN
ACCESSION NUMBER: 2001368401 EMBASE
TITLE: Effects of topical corticosteroid and combined mediator
blockade on domiciliary and laboratory measurements of
nasal function in seasonal allergic rhinitis.
AUTHOR: Wilson A.M.; Sims E.J.; Orr L.C.; Coutie W.J.R.; White
P.S.; Gardiner Q.; Lipworth B.J.
CORPORATE SOURCE: Dr. B.J. Lipworth, Asthma and Allergy Research Group,
Department of Clinical Pharmacology, Ninewells Hospital,
Dundee DDI 9SY, United Kingdom. b.j.lipworth@dundee.ac.uk
SOURCE: Annals of Allergy, Asthma and Immunology, (2001) Vol. 87,
No. 4, pp. 344-349.
Refs: 36
ISSN: 1081-1206 CODEN: ALAIF6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 011 Otorhinolaryngology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English

```

SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 2 Nov 2001
 Last Updated on STN: 2 Nov 2001

CT Medical Descriptors:
 adult
 *allergic rhinitis: DT, drug therapy
 article
 asthma: DT, drug therapy
 clinical article
 clinical trial
 controlled study
 crossover procedure
 drug effect
 female
 home care
 human
 inflammation
 laboratory test
 male
 *mediator release
 nose airway resistance
 pollen allergy
 priority journal
 randomized controlled trial
 respiratory airflow
 rhinomanometry
 rhinometry
 seasonal variation
 single blind procedure
 symptomatology
 *budesonide: CT, clinical trial
 *budesonide: CB, drug combination
 *budesonide: DO, . . .
 RN (budesonide) **51333-22-3**; (cetirizine) **83881-51-0**,
 83881-52-1; (montelukast) 151767-02-1, **158966-92-8**

L21 ANSWER 92 OF 100 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2001071359 EMBASE
 TITLE: Effects of monotherapy with intra-nasal corticosteroid or combined oral histamine and leukotriene receptor antagonists in seasonal allergic rhinitis.
 AUTHOR: Wilson A.M.; Orr L.C.; Sims E.J.; Lipworth B.J.
 CORPORATE SOURCE: B.J. Lipworth, Asthma/Allergy Research Group, Dept. Clin. Pharmacol./Therapeut., Ninewells Hosp./Medical School, Dundee DD1 9SY, United Kingdom
 SOURCE: Clinical and Experimental Allergy, (2001) Vol. 31, No. 1, pp. 61-68.
 Refs: 31
 ISSN: 0954-7894 CODEN: CLEAEN
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 011 Otorhinolaryngology
 026 Immunology, Serology and Transplantation
 037 Drug Literature Index
 039 Pharmacy
 LANGUAGE: English

SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 16 Mar 2001
 Last Updated on STN: 16 Mar 2001

CT Medical Descriptors:
 adult
 *allergic rhinitis: DT, drug therapy
 article
 clinical article
 clinical trial
 controlled study
 crossover procedure
 drug efficacy
 eosinophil
 human
 human experiment
 hydrocortisone urine level
 inflammation
 monotherapy
 nose airflow
 pollen
 priority journal
 randomized controlled trial
 rhinomanometry
 rhinometry
 single blind procedure
 treatment outcome
 *antihistaminic agent: CT, clinical trial
 *antihistaminic agent: AD, drug administration
 *antihistaminic agent: CB, drug combination
 *antihistaminic. . .
 RN (beclometasone dipropionate) 5534-09-8; (budesonide) **51333-22-3**;
 (cetirizine) **83881-51-0**, 83881-52-1; (chlorpheniramine)
 132-22-9; (loratadine) **79794-75-5**; (mometasone furoate)
 83919-23-7; (montelukast) 151767-02-1, **158966-92-8**; (nitric
 oxide) 10102-43-9; (terfenadine) 50679-08-8; (triamcinolone) 124-94-7;
 (zafirlukast) **107753-78-6**

L21 ANSWER 93 OF 100 MEDLINE on STN DUPLICATE 25
 ACCESSION NUMBER: 2001025999 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11029334
 TITLE: Antiasthmatic effects of mediator blockade versus topical
 corticosteroids in allergic rhinitis and asthma.
 AUTHOR: Wilson A M; Orr L C; Sims E J; Dempsey O J; Lipworth B J
 CORPORATE SOURCE: Asthma and Allergy Research Group, Department of Clinical
 Pharmacology and Therapeutics, Ninewells Hospital and
 Medical School, University of Dundee, Dundee, Scotland,
 United Kingdom.
 SOURCE: American journal of respiratory and critical care medicine,
 (2000 Oct) Vol. 162, No. 4 Pt 1, pp. 1297-301.
 Journal code: 9421642. ISSN: 1073-449X.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: (CLINICAL TRIAL)
 (COMPARATIVE STUDY)
 Journal; Article; (JOURNAL ARTICLE)
 (RANDOMIZED CONTROLLED TRIAL)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
 ENTRY MONTH: 200011
 ENTRY DATE: Entered STN: 22 Mar 2001
 Last Updated on STN: 22 Mar 2001
 Entered Medline: 15 Nov 2000

CT . . . & dosage
 Cetirizine: AE, adverse effects
 Cross-Over Studies
 Double-Blind Method
 Drug Therapy, Combination
 Forced Expiratory Volume: DE, drug effects
 Humans

***Inflammation Mediators: AI, antagonists & inhibitors**

*Leukotriene Antagonists: AD, administration & dosage
 Leukotriene Antagonists: AE, adverse effects
 *Quinolines: AD, administration & . . .

RN **158966-92-8 (montelukast); 51333-22-3 (Budesonide);
 83881-51-0 (Cetirizine)**

CN 0 (Acetates); 0 (Anti-Asthmatic Agents); 0 (**Inflammation
 Mediators**); 0 (Leukotriene Antagonists); 0 (Quinolines)

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ACCESSION NUMBER: 2000350797 EMBASE
 TITLE: Allergic **inflammation** in the unified airway:
 Start with the nose.
 AUTHOR: Lipworth B.J.; White P.S.
 CORPORATE SOURCE: Prof. B.J. Lipworth, Asthma and Allergy Research Group,
 Dept. of Clinic. Pharmacol./Therap., Ninewells Hosp. and
 Medical School, Dundee DD1 9SY, United Kingdom.
 b.j.lipworth@dundee.ac.uk
 SOURCE: Thorax, (2000) Vol. 55, No. 10, pp. 878-881.
 Refs: 36
 ISSN: 0040-6376 CODEN: THORA7
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 011 Otorhinolaryngology
 015 Chest Diseases, Thoracic Surgery and Tuberculosis
 037 Drug Literature Index
 LANGUAGE: English
 ENTRY DATE: Entered STN: 26 Oct 2000
 Last Updated on STN: 26 Oct 2000

TI Allergic **inflammation** in the unified airway: Start with the nose.

RN (beclometasone) 4419-39-0; (budesonide) **51333-22-3**; (cetirizine) **83881-51-0**, 83881-52-1; (loratadine) **79794-75-5**;
 (montelukast) 151767-02-1, **158966-92-8**; (zafirlukast) **107753-78-6**

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ACCESSION NUMBER: 2000198310 EMBASE
 TITLE: Allergic rhinitis.
 AUTHOR: Virant F.S.
 CORPORATE SOURCE: Dr. F.S. Virant, Northwest Asthma and Allergy Center, 4540
 Sand Point Way NE, Seattle, WA 98105, United States
 SOURCE: Immunology and Allergy Clinics of North America, (2000)

Vol. 20, No. 2, pp. 265-282.

Refs: 62

ISSN: 0889-8561 CODEN: INCAEP

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 005 General Pathology and Pathological Anatomy

039 Pharmacy

038 Adverse Reactions Titles

037 Drug Literature Index

036 Health Policy, Economics and Management

026 Immunology, Serology and Transplantation

011 Otorhinolaryngology

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 30 Jun 2000

Last Updated on STN: 30 Jun 2000

- AB . . . may play a primary pathophysiologic role in otitis media, sinusitis, and asthma. These secondary disorders occur because of upper airway **inflammation** and the release of various vasoactive mediators, including histamine, prostaglandins, and leukotrienes. The management of allergic rhinitis includes environmental controls. . .
- RN (astemizole) 68844-77-9; (azelastine) **58581-89-8**, 79307-93-0; (beclometasone) 4419-39-0; (brompheniramine) 86-22-6, 980-71-2; (budesonide) **51333-22-3**; (cetirizine) **83881-51-0**, 83881-52-1; (chlorpheniramine) 132-22-9; (clemastine) 15686-51-8; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (cyproheptadine) 129-03-3, 969-33-5; (diphenhydramine) 147-24-0, 58-73-1; (fexofenadine) **138452-21-8**; (flunisolide) 3385-03-3; (fluticasone) 90566-53-3; (histamine) 51-45-6, 56-92-8, 93443-21-1; (hydroxyzine) 2192-20-3, 64095-02-9, 68-88-2; (immunoglobulin E) 37341-29-0; (loratadine) **79794-75-5**; (mometasone furoate) 83919-23-7; (terfenadine) 50679-08-8; (triamcinolone) 124-94-7; (tripelennamine) 154-69-8, 91-81-6; (triprolidine) 486-12-4, 550-70-9; (zileuton) **111406-87-2**, 132880-11-6

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ACCESSION NUMBER: 1999303030 EMBASE

TITLE: [Histamine and leukotrienes in allergic rhinitis].
HISTAMIN UND LEUKOTRIENE BEI DER ALLERGISCHEN RHINITIS.

AUTHOR: Bachert C.; Lange B.

CORPORATE SOURCE: B. Bachert, Kliniek Neus-, Keel- en Oorheelkunde, UZ Gent,
De Pintelaan 185, B-9000 Gent, Belgium

SOURCE: Allergologie, (Aug 1999) Vol. 22, No. 8, pp. 492-507.

Refs: 105

ISSN: 0344-5062 CODEN: ALLRDI

COUNTRY: Germany

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 011 Otorhinolaryngology

026 Immunology, Serology and Transplantation

030 Clinical and Experimental Pharmacology

037 Drug Literature Index

LANGUAGE: German

SUMMARY LANGUAGE: English; German

ENTRY DATE: Entered STN: 10 Sep 1999

Last Updated on STN: 10 Sep 1999

- AB . . . or eosinophils, and mechanisms like the adhesion cascade. This

has led to the realization that allergic rhinitis is a persistent **inflammation**. While histamine is still considered the most important mediator of early phase reaction and mainly responsible for the symptoms sneezing, . . .

- RN. . . 3 hydroxy 2 propylphenoxy)propylthiolphenyl 4 hydroxy 3 methylbutyric acid) 91542-58-4; (alpha methyl 6 (2 quinolylmethoxy) 2 naphthylacetic acid) 133304-99-1; (azelastine) **58581-89-8**, 79307-93-0; (budesonide) **51333-22-3**; (cetirizine) **83881-51-0**, 83881-52-1; (docebenone) 80809-81-0; (ebastine) 90729-43-4; (leukotriene B4) 71160-24-2; (leukotriene C4) 72025-60-6; (leukotriene D4) 73836-78-9; (leukotriene E4) 75715-89-8; (loratadine) **79794-75-5**; (mizolastine) 108612-45-9; (montelukast) 151767-02-1, **158966-92-8**; (piriprost) 79672-88-1; (pobilukast) **107023-41-6**, 108116-15-0; (pranlukast) 103177-37-3; (terfenadine) 50679-08-8; (verlukast) 115104-28-4; (zafirlukast) **107753-78-6**; (zileuton) **111406-87-2**, 132880-11-6
- L21 ANSWER 97 OF 100 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
- ACCESSION NUMBER: 1999174097 EMBASE
- TITLE: American Academy of Asthma, Allergy and Immunology - 55th Annual Meeting: 26 February - 3 March 1999, Orlando, FL, USA.
- AUTHOR: Lieberman P.
- CORPORATE SOURCE: P. Lieberman, Division of Allergy and Immunology, Univ. of Tennessee Coll. of Medicine, 300 Walnut Bend Road 50, Cordova, TN 38018, United States. asthma@memphis@msn.com
- SOURCE: IDrugs, (1999) Vol. 2, No. 5, pp. 405-409. ISSN: 1369-7056 CODEN: IDRUFN
- COUNTRY: United Kingdom
- DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
- FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
007 Pediatrics and Pediatric Surgery
- LANGUAGE: English
- SUMMARY LANGUAGE: English
- ENTRY DATE: Entered STN: 10 Jun 1999
Last Updated on STN: 10 Jun 1999
- AB . . . 984 original oral and poster presentations and over 100 symposia, seminars and workshops. The plenary sessions involved sections on allergic **inflammation**, immune modulation, chemokine receptors, the origins of asthma, the diagnosis and management of food and drug reactions, the environmental influences. . .
- RN (4 [2 [3 (cyclopentyl) 4 methoxyphenyl] 2 phenylethyl]pyridine) 162542-90-7; (azelastine) **58581-89-8**, 79307-93-0; (beclomethasone dipropionate) 5534-09-8; (budesonide) **51333-22-3**; (cetirizine) **83881-51-0**, 83881-52-1; (cilomilast) 153259-65-5; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (ebastine) 90729-43-4; (epinastine) 80012-43-7; (fexofenadine) **138452-21-8**; (fluticasone propionate) **80474-14-2**; (fluticasone) 90566-53-3; (loratadine) **79794-75-5**; (montelukast) 151767-02-1, **158966-92-8**; (piclamilast) 144035-83-6; (rapamycin) 53123-88-9; (recombinant intercellular adhesion molecule 1) 155576-45-7; (rolipram) 61413-54-5; (salbutamol) 18559-94-9; (salmeterol) 89365-50-4; (seratrodast) 103186-19-2, 112665-43-7; (terfenadine) 50679-08-8;

(zafirlukast) **107753-78-6**

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ACCESSION NUMBER: 1997186601 EMBASE

TITLE: Asthma, allergic **inflammation** and new therapeutic strategies.

AUTHOR: Ciprandi G.

SOURCE: Drug News and Perspectives, (1997) Vol. 10, No. 3, pp. 161-165.

ISSN: 0214-0934 CODEN: DNPEED

COUNTRY: Spain

DOCUMENT TYPE: Journal; Conference Article; (Conference paper)

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis

026 Immunology, Serology and Transplantation

037 Drug Literature Index

LANGUAGE: English

ENTRY DATE: Entered STN: 10 Jul 1997

Last Updated on STN: 10 Jul 1997

TI Asthma, allergic **inflammation** and new therapeutic strategies.

RN (azelastine) **58581-89-8**, 79307-93-0; (beclomethasone dipropionate) 5534-09-8; (budesonide) **51333-22-3**; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (fexofenadine) **138452-21-8**; (fluticasone) 90566-53-3; (ipratropium bromide) 22254-24-6; (loratadine) **79794-75-5**; (mometasone furoate) 83919-23-7; (nedocromil) 69049-73-6; (prednisone) 53-03-2; (triamcinolone acetonide) 76-25-5; (zafirlukast) **107753-78-6**; (zanamivir) 139110-80-8; (zileuton) **111406-87-2**, 132880-11-6

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ACCESSION NUMBER: 1996203538 EMBASE

TITLE: Prospects for the development of new drugs for the therapy of respiratory diseases.

AUTHOR: Whelan C.J.

CORPORATE SOURCE: C.J. Whelan, Division of Biosciences, School of Natural Sciences, University of Hertfordshire, Hatfield, Herts AL10 9AB, United Kingdom

SOURCE: Drugs of Today, (1996) Vol. 32, No. 4, pp. 295-311.

Refs: 133

ISSN: 0025-7656 CODEN: MDACAP

COUNTRY: Spain

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis

030 Clinical and Experimental Pharmacology

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 21 Aug 1996

Last Updated on STN: 21 Aug 1996

AB . . . or inhibitors of neutrophil recruitment and activation should offer an approach to the design of drugs which selectively target the **inflammation** associated with these diseases.

RN (apafant) 105219-56-5; (azelastine) **58581-89-8**, 79307-93-0; (beclomethasone dipropionate) 5534-09-8; (cetirizine) **83881-51-0**, 83881-52-1; (cromakalim) 94470-67-4; (fluticasone propionate) **80474-14-2**; (formoterol) 73573-87-2; (interleukin 8) 114308-91-7;

(ipratropium bromide) 22254-24-6; (mifepristone) 84371-65-3; (modipafant) 122956-68-7; (salbutamol) 18559-94-9; (salmeterol) 89365-50-4; (siguazodan) 115344-47-3; (terbutaline) 23031-25-6; (theophylline) 58-55-9, 5967-84-0, 8055-07-0, 8061-56-1, 99007-19-9; (vapiprost) 85505-64-2; (zafirlukast) **107753-78-6**; (zardaverine) 101975-10-4

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ACCESSION NUMBER: 1992359918 EMBASE
 TITLE: Atopic disease in children.
 AUTHOR: Bocian R.C.; Umetsu D.T.
 CORPORATE SOURCE: Dr. R.C. Bocian, Division of Allergy, Department of Pediatrics, Stanford University Medical Center, Stanford, CA 94305-5119, United States
 SOURCE: Current Opinion in Pediatrics, (1992) Vol. 4, No. 6, pp. 1008-1016.
 ISSN: 1040-8703 CODEN: COPEE9
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
 026 Immunology, Serology and Transplantation
 037 Drug Literature Index
 038 Adverse Reactions Titles
 007 Pediatrics and Pediatric Surgery
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 10 Jan 1993
 Last Updated on STN: 10 Jan 1993

CT Medical Descriptors:
 *allergic . . . DT, drug therapy
 *atopy: ET, etiology
 bronchus reactivity
 cigarette smoking
 drug efficacy
 drug safety
 eosinophil
 *food allergy: DT, drug therapy
 *food allergy: ET, etiology
 human
 hypertension: SI, side effect
 immunoglobulin blood level
 immunotherapy
 inflammation: DT, drug therapy
 inflammation: ET, etiology
 inhalational drug administration
 intravenous drug administration
 liver toxicity: SI, side effect
 mast cell degranulation
 mite
 nephrotoxicity: SI, side effect
 prick test
 review
 T lymphocyte
 adrenalin: AD, drug. . .

RN (adrenalin) 51-43-4, 55-31-2, 6912-68-1; (aminophylline) 317-34-0;
 (azelastine) **58581-89-8**, 79307-93-0; (beclometasone dipropionate) 5534-09-8; (budesonide) **51333-22-3**; (cetirizine)

83881-51-0, 83881-52-1; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (cyclosporin A) 59865-13-3, 63798-73-2; (fenoterol) 13392-18-2, 1944-12-3; (gamma interferon) 82115-62-6; (immunoglobulin E) 37341-29-0; (immunoglobulin) 9007-83-4; (ketotifen) 34580-13-7; (methotrexate) 15475-56-6, 59-05-2, 7413-34-5; (methylprednisolone) 6923-42-8, 83-43-2; (nedocromil) 69049-73-6; (orciprenaline) 586-06-1, 5874-97-5; (pobilukast) **107023-41-6**, 108116-15-0; (terbutaline) 23031-25-6; (theophylline) 58-55-9, 5967-84-0, 8055-07-0, 8061-56-1, 99007-19-9

=> d his

(FILE 'HOME' ENTERED AT 08:55:09 ON 03 MAR 2008)

FILE 'REGISTRY' ENTERED AT 08:55:39 ON 03 MAR 2008

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L1      0 S MONTLUKAST/CN
L2      1 S MONTELUKAST/CN
L3      1 S ZILEUTON/CN
L4      1 S ZAFIRLUKAST/CN
L5      4 S ?LUKAST
L6      1 S FLUTICASONE PROPIONATE/CN
L7      0 S MOMETASONE FUORATE MONOHYDRATE/CN
L8      1 S MOMETASONE/CN
L9      1 S BUDESONIDE/CN
L10     1 S AZELASTINE/CN
L11     1 S CETIRIZINE/CN
L12     6 S FEXOFENADINE
L13     2 S LORATADINE
L14     2 S DESLORATADINE
```

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CAPLUS, DDFB, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ESBIODASE, IFIPAT, IMSDRUGNEWS, IMSPRODUCT, IPA, KOSMET, LIFESCI, MEDLINE, NAPRALERT, NLDB, NUTRACEUT, PASCAL, PCTGEN, PHARMAML, ...' ENTERED AT 09:06:08 ON 03 MAR 2008

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L15     11824 S L2 OR L3 OR L4 OR L5
L16     32489 S L6 OR L8 OR L9
L17     32316 S L10 OR L11 OR L12 OR L13 OR L14
L18     2287254 S C REACTIVE PROTEIN OR INFLAMMATION
L19     420 S L15 AND L16 AND L17
L20     128 S L18 AND L19
L21     100 DUP REM L20 (28 DUPLICATES REMOVED)
```

=> s c reactive protein

8 FILES SEARCHED...

33 FILES SEARCHED...

L22 161485 C REACTIVE PROTEIN

=> s l21 and l22

35 FILES SEARCHED...

L23 10 L21 AND L22

=> d l23 1-10 ibib, kwic

L23 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2008 ACS ON STN

ACCESSION NUMBER: 2004:802553 CAPLUS
 DOCUMENT NUMBER: 141:289088
 TITLE: Protocol for improving vision
 INVENTOR(S): Mullally, John P.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 5 pp., Cont.-in-part of U.S.
 Ser. No. 798,017.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004192660	A1	20040930	US 2004-820264	20040408
CA 2518409	A1	20040923	CA 2004-2518409	20040311
CA 2559276	A1	20050929	CA 2005-2559276	20050311
WO 2005089171	A2	20050929	WO 2005-US7804	20050311
WO 2005089171	A3	20060209		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,
 SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF,
 CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM,
 KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG,
 KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:
 US 2003-453917P P 20030312
 US 2003-461534P P 20030409
 US 2003-482574P P 20030624
 US 2004-798017 A2 20040311
 WO 2004-US7381 W 20040311
 WO 2005-US7804 W 20050311

AB A method and composition for reducing highly sensitive C-
reactive protein to improve the vision of a user is
 achieved through the daily administration of a leukotriene inhibitor, and
 antihistamine and. . .
 IT Vision
 (agents to improve; method and composition for reducing highly sensitive
C-reactive protein to improve the vision)
 IT Mycobacterium tuberculosis
 (attenuated; method and composition for reducing highly sensitive C
-reactive protein to improve the vision)
 IT Drug delivery systems
 (capsules; method and composition for reducing highly sensitive C-
reactive protein to improve the vision)
 IT Streptococcus pneumoniae
 (conjugate vaccine; method and composition for reducing highly sensitive
C-reactive protein to improve the vision)
 IT Polysaccharides, biological studies
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (conjugates, pneumococcal; method and composition for reducing highly

- sensitive **C-reactive protein** to improve the vision)
- IT Drug delivery systems
(infusions, nasal; method and composition for reducing highly sensitive **C-reactive protein** to improve the vision)
- IT Antihistamines
Combination chemotherapy
Diabetes mellitus
Eye, disease
Human
Influenza virus
Mixtures
Vaccines
(method and composition for reducing highly sensitive **C-reactive protein** to improve the vision)
- IT **C-reactive protein**
Leukotrienes
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method and composition for reducing highly sensitive **C-reactive protein** to improve the vision)
- IT Corticosteroids, biological studies
Steroids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method and composition for reducing highly sensitive **C-reactive protein** to improve the vision)
- IT Drug delivery systems
(nasal, infusion; method and composition for reducing highly sensitive **C-reactive protein** to improve the vision)
- IT Drug delivery systems
(oral; method and composition for reducing highly sensitive **C-reactive protein** to improve the vision)
- IT 51-30-9, Isoproterenol hydrochloride 53-03-2, Prednisone 54-11-5, Nicotine 54-85-3, Isoniazid 58-55-9, Theophylline, biological studies 61-72-3, Cloxacillin 69-53-4, Ampicillin 74-55-5, Ethambutol 76-25-5, Triamcinolone acetonide 98-96-4, Pyrazinamide 114-07-8, Erythromycin 317-34-0, Aminophylline 564-25-0, Doxycycline 586-06-1, Orciprenaline 1400-61-9, Nystatin 1406-05-9, Penicillin 1944-12-3, Fenoterol hydrobromide 3385-03-3, Flunisolide 4499-40-5, Oxitriphylline, biological studies 5534-09-8, Beclomethasone dipropionate 10118-90-8, Minocycline 13292-46-1, Rifampin 15686-71-2, Cephalixin 15826-37-6, Sodium cromoglycate 18323-44-9, Clindamycin 18559-94-9, Salbutamol 22254-24-6, Ipratropium bromide 23031-32-5, Terbutaline sulfate 26787-78-0, Amoxicillin 31677-93-7, Bupropion hydrochloride 33817-20-8, Pivampicillin 34580-13-7, Ketotifen 43229-80-7, Formoterol fumarate 50370-12-2, Cefadroxil 50679-08-8, Terfenadine 50972-17-3, Bacampicillin 51022-70-9, Albuterol sulfate **51333-22-3**, Budesonide 53994-73-3, Cefaclor **58581-89-8**, Azelastine 64544-07-6, Cefuroxime axetil 65277-42-1, Ketoconazole 65652-44-0, Pirbuterol acetate 68844-77-9, Astemizole 69049-74-7, Nedocromil sodium 79350-37-1, Cefixime **79794-75-5**, Loratadine **80474-14-2**, Fluticasone propionate 81103-11-9, Clarithromycin 82419-36-1, Ofloxacin **83799-24-0**, Fexofenadine **83881-51-0**, Cetirizine 83905-01-5, Azithromycin 84625-61-6, Itraconazole 86386-73-4, Fluconazole 92665-29-7, Cefprozil 93107-08-5, Ciprofloxacin hydrochloride 94749-08-3, Salmeterol xinafoate 100986-85-4, Levofloxacin **107753-78-6**, Zafirlukast

112811-59-3, Gatifloxacin 139110-80-8, Zanamivir 141646-00-6,
 Mometasone furoate monohydrate 151096-09-2, Moxifloxacin 151767-02-1,
 Montelukast sodium 196618-13-0, Oseltamivir 756819-03-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

(method and composition for reducing highly sensitive C-
reactive protein to improve the vision)

L23 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:759824 CAPLUS

DOCUMENT NUMBER: 141:254560

TITLE: Composition and method using a leukotriene inhibitor,
 an antihistamine and a corticosteroid for treating
inflammation by reducing C-
reactive protein

INVENTOR(S): Mullally, John P.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 8 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004180868	A1	20040916	US 2004-798117	20040311
CA 2518409	A1	20040923	CA 2004-2518409	20040311
WO 2004080414	A2	20040923	WO 2004-US7381	20040311
WO 2004080414	A3	20050512		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, HK, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2003-453917P P 20030312
 US 2003-482574P P 20030624
 WO 2004-US7381 W 20040311

TI Composition and method using a leukotriene inhibitor, an antihistamine and a corticosteroid for treating **inflammation** by reducing C-
reactive protein

AB A method and composition for reducing C-**reactive protein** for reducing systemic **inflammation** in the body of a user is achieved through the daily administration of a leukotriene inhibitor, an antihistamine, and a . . .

ST leukotriene inhibitor antihistamine corticosteroid **inflammation**
 treatment C **reactive protein**

IT Mycobacterium tuberculosis
 (attenuated; leukotriene inhibitor, antihistamine, and corticosteroid for treating **inflammation** by reducing C-
reactive protein)

- IT Vaccines
(influenza virus; leukotriene inhibitor, antihistamine, and corticosteroid for treating **inflammation** by reducing **C-reactive protein**)
- IT Drug delivery systems
(infusions; leukotriene inhibitor, antihistamine, and corticosteroid for treating **inflammation** by reducing **C-reactive protein**)
- IT Anti-inflammatory agents
Antihistamines
Combination chemotherapy
Drug delivery systems
Human
Inflammation
(leukotriene inhibitor, antihistamine, and corticosteroid for treating **inflammation** by reducing **C-reactive protein**)
- IT **C-reactive protein**
Glycerides, biological studies
High-density lipoproteins
Leukotrienes
Low-density lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(leukotriene inhibitor, antihistamine, and corticosteroid for treating **inflammation** by reducing **C-reactive protein**)
- IT Corticosteroids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(leukotriene inhibitor, antihistamine, and corticosteroid for treating **inflammation** by reducing **C-reactive protein**)
- IT Drug delivery systems
(nasal; leukotriene inhibitor, antihistamine, and corticosteroid for treating **inflammation** by reducing **C-reactive protein**)
- IT Drug delivery systems
(oral; leukotriene inhibitor, antihistamine, and corticosteroid for treating **inflammation** by reducing **C-reactive protein**)
- IT Streptococcus pneumoniae
(pneumococcal conjugate vaccine; leukotriene inhibitor, antihistamine, and corticosteroid for treating **inflammation** by reducing **C-reactive protein**)
- IT Polysaccharides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pneumococcal polysaccharide vaccine; leukotriene inhibitor, antihistamine, and corticosteroid for treating **inflammation** by reducing **C-reactive protein**)
- IT **Inflammation**
Respiratory system, disease
(sinusitis; leukotriene inhibitor, antihistamine, and corticosteroid for treating **inflammation** by reducing **C-reactive protein**)
- IT Influenza virus
(vaccine; leukotriene inhibitor, antihistamine, and corticosteroid for

treating inflammation by reducing C-reactive protein)

- IT 57-88-5, Cholesterol, biological studies 9004-10-8, Insulin, biological studies 62572-11-6, Hemoglobin Alc
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (leukotriene inhibitor, antihistamine, and corticosteroid for treating inflammation by reducing C-reactive protein)
- IT 51-30-9, Isoproterenol hydrochloride 53-03-2, Prednisone 54-11-5, Nicotine 54-31-9, Lasix 54-85-3, Isoniazid 58-55-9, Theophylline, biological studies 61-72-3, Cloxacillin 69-53-4, Ampicillin 74-55-5, Ethambutol 76-25-5, Triamcinolone acetonide 98-96-4, Pyrazinamide 114-07-8, Erythromycin 317-34-0, Aminophylline 564-25-0, Doxycycline 586-06-1, Orciprenaline 1400-61-9, Nystatin 1406-05-9, Penicillin 1944-12-3, Fenoterol hydrobromide 3385-03-3, Flunisolide 4499-40-5, Oxitriptyline, biological studies 5534-09-8, Beclomethasone dipropionate 10118-90-8, Mincycline 13292-46-1, Rifampin 15686-71-2, Cephalixin 15826-37-6, Sodium cromoglycate 18323-44-9, Clindamycin 18559-94-9, Salbutamol 22254-24-6, Ipratropium bromide 23031-32-5, Terbutaline sulfate 26787-78-0, Amoxicillin 31677-93-7, Bupropion hydrochloride 33817-20-8, Pivampicillin 34580-13-7, Ketotifen 43229-80-7, Formoterol fumarate 50370-12-2, Cefadroxil 50679-08-8, Terfenadine 50972-17-3, Bacampicillin 51022-70-9, Albuterol sulfate **51333-22-3**, Budesonide 53994-73-3, Cefaclor **58581-89-8**, Azelastine. 64544-07-6, Cefuroxime axetil 65277-42-1, Ketoconazole 65652-44-0, Pirbuterol acetate 68844-77-9, Astemizole 69049-74-7, Nedocromil sodium 79307-93-0, Astelin 79350-37-1, Cefixime **79794-75-5**, Loratadine 79902-63-9, Zocor **80474-14-2**, Fluticasone propionate 81103-11-9, Clarithromycin 82419-36-1, Ofloxacin **83799-24-0**, Fexofenadine **83881-51-0**, Cetirizine 83905-01-5, Azithromycin 84625-61-6, Itraconazole 86386-73-4, Fluconazole 92665-29-7, Cefprozil 93107-08-5, Ciprofloxacin hydrochloride 94749-08-3, Salmeterol xinafoate 100986-85-4, Levofloxacin 105816-04-4, Starlix 107133-36-8, Aceon **107753-78-6**, Zafirlukast 112811-59-3, Gatifloxacin 135062-02-1, Prandin 139110-80-8, Zanamivir 141646-00-6, Mometasone furoate monohydrate 151096-09-2, Moxifloxacin 151767-02-1, Montelukast sodium **153439-40-8**, Allegra 155141-29-0, Avandia 156154-37-9, Hyzaar 196618-13-0, Oseltamivir 338752-31-1, Glucovance 756819-03-1
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (leukotriene inhibitor, antihistamine, and corticosteroid for treating inflammation by reducing C-reactive protein)
- L23 ANSWER 3 OF 10 USPATFULL on STN
 ACCESSION NUMBER: 2007:184688 USPATFULL
 TITLE: ETHER DERIVATIVES USEFUL AS INHIBITORS OF PDE4 ISOZYMES
 INVENTOR(S): Marfat, Anthony, 333 Lantern Hill Road, Mystic, CT, UNITED STATES 06378
 Chambers, Robert J., 25 Clipper Drive, Mystic, CT, UNITED STATES 06355
 Magee, Thomas V., 1288 River Road, Mystic, CT, UNITED STATES 06355
 PATENT ASSIGNEE(S): PFIZER INC., New York, NY, UNITED STATES, 10017-5755 (U.S. corporation)

PFIZER PRODUCTS INC., Groton, CT, UNITED STATES, 06340
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2007161681	A1	20070712
APPLICATION INFO.:	US 2007-668915	A1	20070130 (11)
RELATED APPLN. INFO.:	Division of Ser. No. US 2004-918820, filed on 13 Aug 2004, GRANTED, Pat. No. US 7183293 Division of Ser. No. US 2002-66503, filed on 31 Jan 2002, GRANTED, Pat. No. US 6828333		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-265304P	20010131 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	WARNER-LAMBERT COMPANY, 2800 PLYMOUTH RD, ANN ARBOR, MI, 48105, US	
NUMBER OF CLAIMS:	30	
EXEMPLARY CLAIM:	1	
LINE COUNT:	7866	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		
SUMM	. . . for more selective inhibitors of PDEs that are able to suppress both immune cell functions in vitro and allergic pulmonary inflammation in vivo, while at the same time having improved side-effect profiles. Within the airways of patients suffering from asthma and. . .	
SUMM	Airflow obstruction and airway inflammation are features of asthma as well as COPD. While bronchial asthma is predominantly characterized by an eosinophilic inflammation , neutrophils appear to play a major role in the pathogenesis of COPD. Thus, PDEs that are involved in smooth muscle. . .	
SUMM	. . . hydrolases from their granules, and the generation of reactive oxygen species, neutrophils contribute to the tissue destruction associated with chronic inflammation , and are further implicated in the pathology of conditions such as emphysema.	
SUMM	. . . 400 mg; Pruniaux et al., "The novel phosphodiesterase inhibitor CI-1018 inhibits antigen-induced lung eosinophilia in sensitized brown-norway rats--comparison with rolipram," Inflammation S-04-6, 1999. CI-1018 has been demonstrated to have good oral bioavailability (57% in the rat) and good oral potency of. . .	
SUMM	. . . arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with inflammation ; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from. . . uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .	
SUMM	In particular, the compounds of Formula (1.0.0) are useful in the treatment of (1) inflammatory diseases and conditions comprising: joint inflammation , rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic	

- glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .
- DETD . . . (1.0.0) is asthma, a chronic, increasingly common disorder encountered worldwide and characterized by intermittent reversible airway obstruction, airway hyper-responsiveness and **inflammation**. The cause of asthma has yet to be determined, but the most common pathological expression of asthma is **inflammation** of the airways, which may be significant even in the airways of patients with mild asthma. Based on bronchial biopsy. . .
- DETD Pulmonary **Inflammation** in Allergic Cynomolgus Monkeys--The ability of the combinations of therapeutic agents of the present invention to inhibit *Ascaris* antigen induced. . .
- DETD . . . use of primates, is that described in Turner et al., "Characterization of a primate model of asthma using anti-allergy/anti-asthma agents," **Inflammation Research** 45 239-245, 1996.
- DETD COPD is characterized by **inflammation** of the airways, as is the case with asthma, but the inflammatory cells that have been found in the bronchoalveolar. . .
- DETD . . . a productive cough; staphylococcus or streptococcal bronchitis which are caused by staphylococci or streptococci; and vesicular bronchitis in which the **inflammation** extends into the alveoli, which are sometimes visible under the pleura as whitish-yellow granulations like millet seeds.
- DETD . . . and T-lymphocytes. A variety of inflammatory mediators is also released by these cells, all of which may contribute to the **inflammation** exhibited in the late phase response.
- DETD . . . al "Effect of AWD 12-281, a new selective PDE-4 inhibitor, luteprednol and beclomethasone in models of allergic rhinitis and airway **inflammation** in brown norway-rats," *Am. J. Respir. Crit. Care Med.* A95, 1999. The compounds D-22888 and AWD-12,281 have already been described. . .
- DETD . . . rhinitis in terms of anatomical proximity as well as a shared etiology and pathogenesis in some cases. Sinusitis is the **inflammation** of a sinus and this condition may be purulent or nonpurulent, as well as acute or chronic. Depending upon the sinus where the **inflammation** is located, the condition is known as ethmoid, frontal, maxillary, or sphenoid sinusitis. The ethmoidal sinus is one type of. . .
- DETD Arthritis is defined as **inflammation** of the joints, and rheumatoid arthritis is a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammatory. . .
- DETD . . . Accordingly, the term "rheumatoid arthritis" includes acute arthritis, which is arthritis marked by pain, heat, redness, and swelling due to **inflammation**, infection, or trauma; acute gouty arthritis, which is acute arthritis associated with gout; chronic inflammatory arthritis, which is **inflammation** of the joints in chronic disorders such as rheumatoid arthritis; degenerative arthritis, which is osteoarthritis; infectious arthritis, which is arthritis. . . or parasites; Lyme arthritis, which is arthritis of the large joints associated with Lyme 20 disease; proliferative arthritis, which is **inflammation** of the joints with proliferation of the synovium, seen in rheumatoid arthritis; psoriatic arthritis, which is a syndrome in which psoriasis occurs in association with inflammatory arthritis; and vertebral arthritis, which is **inflammation** involving the intervertebral disks.
- DETD The three major pathological features of rheumatoid arthritis that are

- responsible for progressive joint destruction are **inflammation**, abnormal cellular and humoral responses, and synovial hyperplasia. The particular cellular pathology of rheumatoid arthritis includes the presence of T-cells. . . disease. Pro-inflammatory cytokines, e.g., IL-1, IL-4, IL-5, IL-6, IL-9, IL-13, and TNF- α , are the major contributors to joint tissue damage, **inflammation**, hyperplasia, pannus formation and bone resorption. See Firestein, G. S. and Zvaifler, W. J., "How important are T-cells in chronic. . .
- DETD . . . of the compounds of Formula (1.0.0) to inhibit TNF- α release from stimulated monocytes can be correlated with animal models of **inflammation** in which anti-inflammatory effects can be shown to correspond to suppression of TNF- α accumulation. One such animal model involves inhibition. . .
- DETD . . . are tophi or chalky deposits of sodium urate. Some therapeutic agents are useful in treating both gout and its attendant **inflammation**, e.g., phenylbutazone and colchicine; while other therapeutic agents possess only uricosuric properties, e.g., sulfinpyrazone and benzbromarone
- DETD . . . to the present invention such fever is either that manifested in pharyngoconjunctival fever or rheumatic fever, or that manifested during **inflammation**. A concomitant of **inflammation** is pain, especially that experienced in the joints and connective tissue of those suffering from rheumatoid arthritis and gout.
- DETD . . . PDE4 inhibitory compounds of Formula (1.0.0) provide beneficial results in the treatment of gout, and fever and pain associated with **inflammation**.
- DETD . . . PDE4 inhibitors and their utility in the treatment of rheumatoid arthritis. The activity of rolipram in animal models of acute **inflammation** such as the mouse adjuvant arthritis model, has been demonstrated in the art; Sekut et al, "Anti-inflammatory activity of phosphodiesterase (PDE) IV inhibitors in acute and chronic models of **inflammation**," Olin. Exp. Immunol. 100(1) 126-132, 1995. The ability of rolipram to reduce disease severity in the collagen 11 induced arthritis. . .
- DETD . . . the compound t.i.d. The compound was able to induce a positive trend towards clinical improvement associated with a reduction in **C-reactive protein** and IL-6 serum levels. Chikanza et al, "The clinical effects of RP73401 phosphodiesterase Type 4 inhibitor in patients with rheumatoid. . .
- DETD . . . a central role in the induction of local IgE responses and the recruitment of eosinophils in this disease. The chronic **inflammation** seen in atopic dermatitis is considered to be the result of several interdependent factors, such as repeated or persistent allergen. . . vascular adhesion molecule-1 (VCAM-1), an adhesion molecule involved in the migration of mononuclear cells and eosinophils into sites of tissue **inflammation**. Further, IL-5 is a key mediator of eosinophil activation, which is a common feature of atopic disease.
- DETD . . . conjunctiva is a delicate membrane that lines the eyelids and covers the exposed surface of the sclera. Conjunctivitis is an **inflammation** of the conjunctiva that generally consists of conjunctival hyperemia associated with a discharge. The most common types of conjunctivitis, which. . . which is an acute conjunctivitis caused by bacteria or viruses, particularly gonococci, meningococci, pneumococci, and streptococci, and characterized by severe **inflammation** of the conjunctiva and copious discharge of pus; and vernal conjunctivitis which is a bilateral conjunctivitis of

- seasonal occurrence, of. . .
- DETD . . . is the vascular middle coat or tunic of the eye, comprising the iris, ciliary body, and choroid. Uveitis is an **inflammation** of all or part of the uvea and commonly involves the other tunics of the eye, i.e., the sclera and. . . the posterior portion, characterized by nodular collections of epithelioid cells and giant cells surrounded by lymphocytes; nongranulomatous uveitis which is **inflammation** of the anterior portion of the uveal tract, i.e., the iris and ciliary body; phacoantigenic uveitis which is one of. . .
- DETD . . . number of mediators via either topical or systemic administration. For example, rolipram has been shown to inhibit croton oil-induced ear **inflammation** in the mouse at topical doses as low as 0.03 mg per ear. The selective PDE4 inhibitor Ro 20-1724 has. . .
- DETD . A sclerosis is an induration, or hardening, and refers especially to hardening of a part from **inflammation**, and from increased formation of connective tissue and in diseases of the interstitial substance. The term "sclerosis" is used chiefly. . .
- DETD Multiple sclerosis is an autoimmune disease that in addition to chronic **inflammation** and demyelination, also results in gliosis within the central nervous system. There are several disease subtypes, including primary progressive multiple. . . subtypes may be distinguished from each other on the basis of the course of the disease, of the type of **inflammation** involved, and through the use of magnetic resonance imaging (MRI). It is also possible for the basic disease mechanism to change during the course of multiple sclerosis, with an **inflammation**-based process being replaced later by one which involves demyelination and axonal damage. See Weillbach and Gold, "Disease modifying treatments for. . .
- DETD . . . compounds of Formula (1.0.0) also possess activity as immunosuppressive agents and are especially useful for treating autoimmune diseases in which **inflammation** is a component part of the autoimmune disease, or in which **inflammation** is part of the etiology of the autoimmune disease, or in which **inflammation** is otherwise involved with the autoimmune disease. Alternatively, the compounds of Formula (1.0.0) are anti-inflammatory agents useful in the treatment. . .
- DETD . . . with the formation of pseudopolyps, i.e., edematous, inflamed islands of mucosa between areas of ulceration; and transmural colitis, which is **inflammation** of the full thickness of the bowel, rather than mucosal and submucosal disease, usually with the formation of noncaseating granulomas. . .
- DETD . . . arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with **inflammation**; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from. . . uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis. . .
- DETD . . . anesthetics for relieving pain, irritation and itching, e.g., benzocaine, lidocaine, dibucaine, and pramoxine hydrochloride; topical analgesics for relieving pain and **inflammation**, e.g., methyl salicylate, camphor, menthol, and resorcinol; topical antiseptics for preventing infection, e.g., benzalkonium chloride and povidone-iodine;

and vitamins and. . .

CLM What is claimed is:

- . . . degenerative arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with **inflammation**; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from the. . .
- . . . conjunctivitis; uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .
- . . . disease, disorder, or condition is a member selected from the group consisting of (1) inflammatory diseases and conditions comprising: joint **inflammation**, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .

IT 50-24-8, Prednisolone 53-03-2, Prednisone 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfapyrazone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 64-86-8, Colchicine 76-25-5, Triamcinolone acetonide 90-82-4, Pseudoephedrine 101-40-6, Propylhexedrine 113-92-8, Chlorpheniramine 128-39-2D, 2,6-Di-tert-butylphenol, hydrazone derivs. 315-30-0, Allopurinol 317-34-0, Aminophylline 404-86-4, Capsaicin 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 586-06-1, Metaproterenol 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride 2315-02-8, Oxymetazoline hydrochloride 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromarone 5534-09-8, Beclomethasone dipropionate 6339-87-3D, Thiophene-2-sulfonamide, derivs. 7440-57-5D, Gold, aurothio derivs. 7683-59-2, Isoproterenol 9004-08-4D, Cathepsin, derivs. 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate 18559-94-9, Albuterol 22254-24-6, Ipratropium bromide 23031-25-6, Terbutaline 28797-61-7, Pirenzepine 30286-75-0, Oxitropium bromide 30392-40-6, Bitolterol 38677-81-5, Pirbuterol **51333-22-3**, Budesonide **58581-89-8**, Azelastine 59865-13-3, Cyclosporine 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide **79794-75-5**, Loratadine **80474-14-2**, Fluticasone propionate 80880-90-6, Telenzepine **83799-24-0**, Fexofenadine 83869-56-1, Granulocyte-macrophage colony-stimulating factor **83881-51-0**, Cetirizine 83919-23-7, Mometasone furoate 89365-50-4, Salmeterol 93211-49-5, L-651392 96566-25-5, Ablukast **100643-71-8**, Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin 106096-93-9, Basic fibroblast growth factor **107753-78-6**, Zafirlukast **111406-87-2**, Zileuton 118414-82-7, MK-886 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide 128253-31-6, BAY x 1005 128312-51-6 136310-93-5, Tiotropium bromide 140841-32-3 141579-54-6, Fenleuton 141579-87-5 143538-27-6, BAY x 7195 147030-01-1, MK-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast 151581-24-7, Iralukast 154355-76-7, ABT-761 158930-07-5, L-739010 **158966-92-8**, Montelukast 162011-90-7, Rofecoxib 162750-10-9, SB-210661 168154-07-2, L-746530 170277-31-3, Infliximab 171964-73-1, ZD-0892 174636-32-9, Talnetant 185243-69-0, Etanercept 202415-99-4 204974-93-6, BIIL 260 257892-34-5, D 4418 331731-18-1, D 2E7 346735-24-8, BIIL 284 350610-64-9, NKP-608C 446023-33-2, UT

77

(combination therapy with PDE4 inhibitors; preparation of carbamoyl-substituted pyridinyl aryl ether derivs. as inhibitors of PDE4 isoenzymes)

L23 ANSWER 4 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2005:57341 USPATFULL
 TITLE: Ether derivatives useful as inhibitors of PDE4 isozymes
 INVENTOR(S): Marfat, Anthony, Mystic, CT, UNITED STATES
 Chambers, Robert J., Mystic, CT, UNITED STATES
 Magee, Thomas V., Mystic, CT, UNITED STATES
 PATENT ASSIGNEE(S): Pfizer Inc (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005049258	A1	20050303
	US 7183293	B2	20070227
APPLICATION INFO.:	US 2004-918820	A1	20040813 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2002-66503, filed on 31 Jan 2002, GRANTED, Pat. No. US 6828333		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-265304P	20010131 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	PFIZER INC., PATENT DEPARTMENT, MS8260-1611, EASTERN POINT ROAD, GROTON, CT, 06340	
NUMBER OF CLAIMS:	9	
EXEMPLARY CLAIM:	1	
LINE COUNT:	7224	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . for more selective inhibitors of PDEs that are able to suppress both immune cell functions in vitro and allergic pulmonary **inflammation** in vivo, while at the same time having improved side-effect profiles. Within the airways of patients suffering from asthma and. . .

SUMM [0008] Airflow obstruction and airway **inflammation** are features of asthma as well as COPD. While bronchial asthma is predominantly characterized by an eosinophilic **inflammation**, neutrophils appear to play a major role in the pathogenesis of COPD. Thus, PDEs that are involved in smooth muscle. . .

SUMM . . . hydrolases from their granules, and the generation of reactive oxygen species, neutrophils contribute to the tissue destruction associated with chronic **inflammation**, and are further implicated in the pathology of conditions such as emphysema.

SUMM . . . 400 mg; Pruniaux et al., "The novel phosphodiesterase inhibitor Cl-1018 inhibits antigen-induced lung eosinophilia in sensitized brown-norway rats--comparison with rolipram," **Inflammation** 5-04-6, 1999. Cl-1018 has been demonstrated to have good oral bioavailability (57% in the rat) and good oral potency of. . .

SUMM [0200] gout, and fever and pain associated with **inflammation**;

SUMM [0205] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

- SUMM . . . In particular, the compounds of Formula (1.0.0) are useful in the treatment of (1) inflammatory diseases and conditions comprising: joint **inflammation**, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .
- DETD . . . (1.0.0) is asthma, a chronic, increasingly common disorder encountered worldwide and characterized by intermittently reversible airway obstruction, airway hyper-responsiveness and **inflammation**. The cause of asthma has yet to be determined, but the most common pathological expression of asthma is **inflammation** of the airways, which may be significant even in the airways of patients with mild asthma. Based on bronchial biopsy. . .
- DETD [0404] Pulmonary **Inflammation** in Allergic Cynomolgus Monkeys--The ability of the combinations of therapeutic agents of the present invention to inhibit *Ascaris* antigen induced. . .
- DETD . . . use of primates, is that described in Turner et al., "Characterization of a primate model of asthma using anti-allergy/anti-asthma agents," **Inflammation Research** 45 239-245, 1996.
- DETD [0419] COPD is characterized by **inflammation** of the airways, as is the case with asthma, but the inflammatory cells that have been found in the bronchoalveolar. . .
- DETD . . . a productive cough; staphylococcus or streptococcal bronchitis which are caused by staphylococci or streptococci; and vesicular bronchitis in which the **inflammation** extends into the alveoli, which are sometimes visible under the pleura as whitish-yellow granulations like millet seeds.
- DETD . . . and T-lymphocytes. A variety of inflammatory mediators is also released by these cells, all of which may contribute to the **inflammation** exhibited in the late phase response.
- DETD . . . al "Effect of AWD 12-281, a new selective PDE-4 inhibitor, luteprednol and beclomethasone in models of allergic rhinitis and airway **inflammation** in brown norway-rats," *Am. J. Respir. Crit. Care Med.* A95, 1999. The compounds D-22888 and AWD-12,281 have already been described. . .
- DETD . . . rhinitis in terms of anatomical proximity as well as a shared etiology and pathogenesis in some cases. Sinusitis is the **inflammation** of a sinus and this condition may be purulent or nonpurulent, as well as acute or chronic. Depending upon the sinus where the **inflammation** is located, the condition is known as ethmoid, frontal, maxillary, or sphenoid sinusitis. The ethmoidal sinus is one type of. . .
- DETD [0441] Arthritis is defined as **inflammation** of the joints, and rheumatoid arthritis is a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammatory. . .
- DETD . . . Accordingly, the term "rheumatoid arthritis" includes acute arthritis, which is arthritis marked by pain, heat, redness, and swelling due to **inflammation**, infection, or trauma; acute gouty arthritis, which is acute arthritis associated with gout; chronic inflammatory arthritis, which is **inflammation** of the joints in chronic disorders such as rheumatoid arthritis; degenerative arthritis, which is osteoarthritis; infectious arthritis, which is arthritis. . . or parasites; Lyme arthritis, which is arthritis of the large joints associated with Lyme 20 disease; proliferative arthritis, which is **inflammation** of the joints with proliferation of the synovium, seen in rheumatoid arthritis; psoriatic arthritis, which is a syndrome

in which psoriasis occurs in association with inflammatory arthritis; and vertebral arthritis, which is **inflammation** involving the intervertebral disks.

DETD [0443] The three major pathological features of rheumatoid arthritis that are responsible for progressive joint destruction are **inflammation**, abnormal cellular and humoral responses, and synovial hyperplasia. The particular cellular pathology of rheumatoid arthritis includes the presence of T-cells. . . disease. Pro-inflammatory cytokines, e.g., IL-1, IL-4, IL-5, IL-6, IL-9, IL-13, and TNF- α , are the major contributors to joint tissue damage, **inflammation**, hyperplasia, pannus formation and bone resorption. See Firestein, G. S. and Zvaifler, W. J., "How important are T-cells in chronic. . .

DETD . . . of the compounds of Formula (1.0.0) to inhibit TNF- α release from stimulated monocytes can be correlated with animal models of **inflammation** in which anti-inflammatory effects can be shown to correspond to suppression of TNF- α accumulation. One such animal model involves inhibition. . .

DETD . . . are tophi or chalky deposits of sodium urate. Some therapeutic agents are useful in treating both gout and its attendant **inflammation**, e.g., phenylbutazone and colchicine; while other therapeutic agents possess only uricosuric properties, e.g., sulfinpyrazone and benzbromarone

DETD . . . to the present invention such fever is either that manifested in pharyngoconjunctival fever or rheumatic fever, or that manifested during **inflammation**. A concomitant of **inflammation** is pain, especially that experienced in the joints and connective tissue of those suffering from rheumatoid arthritis and gout.

DETD . . . PDE4 inhibitory compounds of Formula (1.0.0) provide beneficial results in the treatment of gout, and fever and pain associated with **inflammation**.

DETD . . . PDE4 inhibitors and their utility in the treatment of rheumatoid arthritis. The activity of rolipram in animal models of acute **inflammation** such as the mouse adjuvant arthritis model, has been demonstrated in the art; Sekut et al, "Anti-inflammatory activity of phosphodiesterase (PDE) IV inhibitors in acute and chronic models of **inflammation**," Olin. Exp. Immunol. 100(1) 126-132, 1995. The ability of rolipram to reduce disease severity in the collagen 11 induced arthritis. . .

DETD . . . the compound t.i.d. The compound was able to induce a positive trend towards clinical improvement associated with a reduction in **C-reactive protein** and IL-6 serum levels.

Chikanza et al, "The clinical effects of RP73401 phosphodiesterase Type 4 inhibitor in patients with rheumatoid. . .

DETD . . . a central role in the induction of local IgE responses and the recruitment of eosinophils in this disease. The chronic **inflammation** seen in atopic dermatitis is considered to be the result of several interdependent factors, such as repeated or persistent allergen. . . vascular adhesion molecule-1 (VCAM-1), an adhesion molecule involved in the migration of mononuclear cells and eosinophils into sites of tissue **inflammation**. Further, IL-5 is a key mediator of eosinophil activation, which is a common feature of atopic disease.

DETD . . . conjunctiva is a delicate membrane that lines the eyelids and covers the exposed surface of the sclera. Conjunctivitis is an **inflammation** of the conjunctiva that generally consists of conjunctival hyperemia associated with a discharge. The most common

- types of conjunctivitis, which. . . which is an acute conjunctivitis caused by bacteria or viruses, particularly gonococci, meningococci, pneumococci, and streptococci, and characterized by severe **inflammation** of the conjunctiva and copious discharge of pus; and vernal conjunctivitis which is a bilateral conjunctivitis of seasonal occurrence, of. . .
- DETD . . . is the vascular middle coat or tunic of the eye, comprising the iris, ciliary body, and choroid. Uveitis is an **inflammation** of all or part of the uvea and commonly involves the other tunics of the eye, i.e., the sclera and. . . the posterior portion, characterized by nodular collections of epithelioid cells and giant cells surrounded by lymphocytes; nongranulomatous uveitis which is **inflammation** of the anterior portion of the uveal tract, i.e., the iris and ciliary body; phacoantigenic uveitis which is one of. . .
- DETD . . . number of mediators via either topical or systemic administration. For example, rolipram has been shown to inhibit croton oil-induced ear **inflammation** in the mouse at topical doses as low as 0.03 mg per ear. The selective PDE4 inhibitor Ro 20-1724 has. . .
- DETD [0474] A sclerosis is an induration, or hardening, and refers especially to hardening of a part from **inflammation**, and from increased formation of connective tissue and in diseases of the interstitial substance. The term "sclerosis" is used chiefly. . .
- DETD [0475] Multiple sclerosis is an autoimmune disease that in addition to chronic **inflammation** and demyelination, also results in gliosis within the central nervous system. There are several disease subtypes, including primary progressive multiple. . . subtypes may be distinguished from each other on the basis of the course of the disease, of the type of **inflammation** involved, and through the use of magnetic resonance imaging (MRI). It is also possible for the basic disease mechanism to change during the course of multiple sclerosis, with an **inflammation**-based process being replaced later by one which involves demyelination and axonal damage. See Weillbach and Gold, "Disease modifying treatments for. . .
- DETD . . . compounds of Formula (1.0.0) also possess activity as immunosuppressive agents and are especially useful for treating autoimmune diseases in which **inflammation** is a component part of the autoimmune disease, or in which **inflammation** is part of the etiology of the autoimmune disease, or in which **inflammation** is otherwise involved with the autoimmune disease. Alternatively, the compounds of Formula (1.0.0) are anti-inflammatory agents useful in the treatment. . .
- DETD . . . with the formation of pseudopolyps, i.e., edematous, inflamed islands of mucosa between areas of ulceration; and transmural colitis, which is **inflammation** of the full thickness of the bowel, rather than mucosal and submucosal disease, usually with the formation of noncaseating granulomas,. . .
- DETD [0518] gout, and fever and pain associated with **inflammation**;
- DETD [0523] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .
- DETD . . . anesthetics for relieving pain, irritation and itching, e.g., benzocaine, lidocaine, dibucaine, and pramoxine hydrochloride; topical analgesics for relieving pain and **inflammation**, e.g., methyl salicylate, camphor, menthol, and resorcinol; topical antiseptics for

preventing infection, e.g., benzalkonium chloride and povidone-iodine; and vitamins and. . .

CLM What is claimed is:

. . . degenerative arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with **inflammation**; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from the. . . conjunctivitis; uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;.

IT 50-24-8, Prednisolone 53-03-2, Prednisone 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfinpyrazone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 64-86-8, Colchicine 76-25-5, Triamcinolone acetonide 90-82-4, Pseudoephedrine 101-40-6, Propylhexedrine 113-92-8, Chlorpheniramine 128-39-2D, 2,6-Di-tert-butylphenol, hydrazine derivs. 315-30-0, Allopurinol 317-34-0, Aminophylline 404-86-4, Capsaicin 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 586-06-1, Metaproterenol 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride 2315-02-8, Oxymetazoline hydrochloride 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromarone 5534-09-8, Beclomethasone dipropionate 6339-87-3D, Thiophene-2-sulfonamide, derivs. 7440-57-5D, Gold, aurothio derivs. 7683-59-2, Isoproterenol 9004-08-4D, Cathepsin, derivs. 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate 18559-94-9, Albuterol 22254-24-6, Ipratropium bromide 23031-25-6, Terbutaline 28797-61-7, Pirenzepine 30286-75-0, Oxtripium bromide 30392-40-6, Bitolterol 38677-81-5, Pirbuterol **51333-22-3**, Budesonide **58581-89-8**, Azelastine 59865-13-3, Cyclosporine 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide **79794-75-5**, Loratadine **80474-14-2**, Fluticasone propionate 80880-90-6, Telenzepine **83799-24-0**, Fexofenadine 83869-56-1, Granulocyte-macrophage colony-stimulating factor **83881-51-0**, Cetirizine 83919-23-7, Mometasone furoate 89365-50-4, Salmeterol 93211-49-5, L-651392 96566-25-5, Ablukast **100643-71-8**, Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin 106096-93-9, Basic fibroblast growth factor **107753-78-6**, Zafirlukast **111406-87-2**, Zileuton 118414-82-7, MK-886 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide 128253-31-6, BAY x 1005 128312-51-6 136310-93-5, Tiotropium bromide 140841-32-3 141579-54-6, Fenleuton 141579-87-5 143538-27-6, BAY x 7195 147030-01-1, MK-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast 151581-24-7, Iralukast 154355-76-7, ABT-761 158930-07-5, L-739010 **158966-92-8**, Montelukast 162011-90-7, Rofecoxib 162750-10-9, SB-210661 168154-07-2, L-746530 170277-31-3, Inflximab 171964-73-1, ZD-0892 174636-32-9, Talnetant 185243-69-0, Etanercept 202415-99-4 204974-93-6, BIIL 260 257892-34-5, D 4418 331731-18-1, D 2E7 346735-24-8, BIIL 284 350610-64-9, NKP-608C 446023-33-2, UT 77

(combination therapy with PDE4 inhibitors; preparation of carbamoyl-substituted pyridinyl aryl ether derivs. as inhibitors of PDE4 isoenzymes)

L23 ANSWER 5 OF 10 USPATFULL on STN
 ACCESSION NUMBER: 2004:64384 USPATFULL
 TITLE: Nicotinamide biaryl derivatives useful as inhibitors of PDE4 isozymes
 INVENTOR(S): Chambers, Robert J., Mystic, CT, UNITED STATES
 Marfat, Anthony, Mystic, CT, UNITED STATES
 Magee, Thomas V., Mystic, CT, UNITED STATES
 PATENT ASSIGNEE(S): Pfizer Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004048903	A1	20040311
	US 6953810	B2	20051011
APPLICATION INFO.:	US 2003-613988	A1	20030702 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2002-62813, filed on 31 Jan 2002, GRANTED, Pat. No. US 6649633		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-265492P	20010131 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	PFIZER INC., PATENT DEPARTMENT, MS8260-1611, EASTERN POINT ROAD, GROTON, CT, 06340	

NUMBER OF CLAIMS: 18
 EXEMPLARY CLAIM: 1
 LINE COUNT: 7041

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . for more selective inhibitors of PDEs that are able to suppress both immune cell functions in vitro and allergic pulmonary **inflammation** in vivo, while at the same time having improved side-effect profiles. Within the airways of patients suffering from asthma and. . .

SUMM [0008] Airflow obstruction and airway **inflammation** are features of asthma as well as COPD. While bronchial asthma is predominantly characterized by an eosinophilic **inflammation**, neutrophils appear to play a major role in the pathogenesis of COPD. Thus, PDEs that are involved in smooth muscle. . .

SUMM . . . hydrolases from their granules, and the generation of reactive oxygen species, neutrophils contribute to the tissue destruction associated with chronic **inflammation**, and are further implicated in the pathology of conditions such as emphysema.

SUMM . . . 400 mg; Pruniaux et al., "The novel phosphodiesterase inhibitor CI-1018 inhibits antigen-induced lung eosinophilia in sensitized brown-norway rats--comparison with rolipram," **Inflammation** S-04-6, 1999, CI-1018 has been demonstrated to have good oral bioavailability (57% in the rat) and good oral potency of. . .

SUMM [0202] gout, and fever and pain associated with **inflammation**;

SUMM [0207] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

SUMM . . . In particular, the compounds of Formula (1.0.0) are useful in the treatment of (1) inflammatory diseases and conditions comprising: joint **inflammation**, rheumatoid arthritis, rheumatoid

- spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .
- SUMM . . . (1.0.0) is asthma, a chronic, increasingly common disorder encountered worldwide and characterized by intermittent reversible airway obstruction, airway hyper-responsiveness and **inflammation**. The cause of asthma has yet to be determined, but the most common pathological expression of asthma is **inflammation** of the airways, which may be significant even in the airways of patients with mild asthma. Based on bronchial biopsy. . .
- SUMM [0393] Pulmonary **Inflammation** in Allergic Cynomolgus Monkeys
- SUMM . . . use of primates, is that described in Turner et al., "Characterization of a primate model of asthma using anti-allergy/anti-asthma agents," **Inflammation Research** 45 239-245, 1996.
- SUMM [0409] COPD is characterized by **inflammation** of the airways, as is the case with asthma, but the inflammatory cells that have been found in the bronchoalveolar. . .
- SUMM . . . a productive cough; staphylococcus or streptococcal bronchitis which are caused by staphylococci or streptococci; and vesicular bronchitis in which the **inflammation** extends into the alveoli, which are sometimes visible under the pleura as whitish-yellow granulations like millet seeds.
- SUMM . . . and T-lymphocytes. A variety of inflammatory mediators is also released by these cells, all of which may contribute to the **inflammation** exhibited in the late phase response.
- SUMM . . . al "Effect of AWD 12-281, a new selective PDE-4 inhibitor, luteprednol and beclomethasone in models of allergic rhinitis and airway **inflammation** in brown norway-rats," Am. J. Respir. Crit. Care Med. A95, 1999. The compounds D-22888 and AWD-12,281 have already been described. . .
- SUMM . . . rhinitis in terms of anatomical proximity as well as a shared etiology and pathogenesis in some cases. Sinusitis is the **inflammation** of a sinus and this condition may be purulent or nonpurulent, as well as acute or chronic. Depending upon the sinus where the **inflammation** is located, the condition is known as ethmoid, frontal, maxillary, or sphenoid sinusitis. The ethmoidal sinus is one type of. . .
- SUMM [0429] Arthritis is defined as **inflammation** of the joints, and rheumatoid arthritis is a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammatory. . .
- SUMM . . . Accordingly, the term "rheumatoid arthritis" includes acute arthritis, which is arthritis marked by pain, heat, redness, and swelling due to **inflammation**, infection, or trauma; acute gouty arthritis, which is acute arthritis associated with gout; chronic inflammatory arthritis, which is **inflammation** of the joints in chronic disorders such as rheumatoid arthritis; degenerative arthritis, which is osteoarthritis; infectious arthritis, which is arthritis. . . or parasites; Lyme arthritis, which is arthritis of the large joints associated with Lyme 20 disease; proliferative arthritis, which is **inflammation** of the joints with proliferation of the synovium, seen in rheumatoid arthritis; psoriatic arthritis, which is a syndrome in which psoriasis occurs in association with inflammatory arthritis; and vertebral arthritis, which is **inflammation** involving the intervertebral disks.
- SUMM [0431] The three major pathological features of rheumatoid arthritis that are responsible for progressive joint destruction are

inflammation, abnormal cellular and humoral responses, and synovial hyperplasia. The particular cellular pathology of rheumatoid arthritis includes the presence of T-cells. . . . disease. Pro-inflammatory cytokines, e.g., IL-1, IL-4, IL-5, IL-6, IL-9, IL-13, and TNF- α , are the major contributors to joint tissue damage, **inflammation**, hyperplasia, pannus formation and bone resorption. See Firestein, G. S. and Zvaifler, W. J., "How important are T-cells in chronic. . . .

SUMM . . . of the compounds of Formula (1.0.0) to inhibit TNF- α release from stimulated monocytes can be correlated with animal models of **inflammation** in which anti-inflammatory effects can be shown to correspond to suppression of TNF- α accumulation. One such animal model involves inhibition. . . .

SUMM . . . are tophi or chalky deposits of sodium urate. Some therapeutic agents are useful in treating both gout and its attendant **inflammation**, e.g., phenylbutazone and colchicine; while other therapeutic agents possess only uricosuric properties, e.g., sulfinpyrazone and benzbromarone

SUMM . . . to the present invention such fever is either that manifested in pharyngoconjunctival fever or rheumatic fever, or that manifested during **inflammation**. A concomitant of **inflammation** is pain, especially that experienced in the joints and connective tissue of those suffering from rheumatoid arthritis and gout.

SUMM . . . PDE4 inhibitory compounds of Formula (1.0.0) provide beneficial results in the treatment of gout, and fever and pain associated with **inflammation**.

SUMM . . . PDE4 inhibitors and their utility in the treatment of rheumatoid arthritis. The activity of rolipram in animal models of acute **inflammation** such as the mouse adjuvant arthritis model, has been demonstrated in the art; Sekut et al, "Anti-inflammatory activity of phosphodiesterase (PDE) IV inhibitors in acute and chronic models of **inflammation**," Olin. Exp. Immunol. 100(1) 126-132, 1995. The ability of rolipram to reduce disease severity in the collagen II induced arthritis. . . .

SUMM . . . the compound t.i.d. The compound was able to induce a positive trend towards clinical improvement associated with a reduction in **C-reactive protein** and IL-6 serum levels. Chikanza et al, "The clinical effects of RP73401 phosphodiesterase Type 4 inhibitor in patients with rheumatoid. . . .

SUMM . . . a central role in the induction of local IgE responses and the recruitment of eosinophils in this disease. The chronic **inflammation** seen in atopic dermatitis is considered to be the result of several interdependent factors, such as repeated or persistent allergen. . . . vascular adhesion molecule-1 (VCAM-1), an adhesion molecule involved in the migration of mononuclear cells and eosinophils into sites of tissue **inflammation**. Further, IL-5 is a key mediator of eosinophil activation, which is a common feature of atopic disease.

SUMM . . . conjunctiva is a delicate membrane that lines the eyelids and covers the exposed surface of the sclera. Conjunctivitis is an **inflammation** of the conjunctiva that generally consists of conjunctival hyperemia associated with a discharge. The most common types of conjunctivitis, which. . . . which is an acute conjunctivitis caused by bacteria or viruses, particularly gonococci, meningococci, pneumococci, and streptococci, and characterized by severe **inflammation** of the conjunctiva and copious discharge of pus; and vernal conjunctivitis which is a bilateral conjunctivitis of

- seasonal occurrence, of. . .
- SUMM . . . is the vascular middle coat or tunic of the eye, comprising the iris, ciliary body, and choroid. Uveitis is an **inflammation** of all or part of the uvea and commonly involves the other tunics of the eye, i.e., the sclera and. . . the posterior portion, characterized by nodular collections of epithelioid cells and giant cells surrounded by lymphocytes; nongranulomatous uveitis which is **inflammation** of the anterior portion of the uveal tract, i.e., the iris and ciliary body; phacoantigenic uveitis which is one of. . .
- SUMM . . . number of mediators via either topical or systemic administration. For example, rolipram has been shown to inhibit croton oil-induced ear **inflammation** in the mouse at topical doses as low as 0.03 mg per ear. The selective PDE4 inhibitor Ro 20-1724 has. . .
- SUMM [0460] A sclerosis is an induration, or hardening, and refers especially to hardening of a part from **inflammation**, and from increased formation of connective tissue and in diseases of the interstitial substance. The term "sclerosis" is used chiefly. . .
- SUMM [0461] Multiple sclerosis is an autoimmune disease that in addition to chronic **inflammation** and demyelination, also results in gliosis within the central nervous system. There are several disease subtypes, including primary progressive multiple. . . subtypes may be distinguished from each other on the basis of the course of the disease, of the type of **inflammation** involved, and through the use of magnetic resonance imaging (MRI). It is also possible for the basic disease mechanism, to change during the course of multiple sclerosis, with an **inflammation**-based process being replaced later by one which involves demyelination and axonal damage. See Weillbach and Gold, "Disease modifying treatments for. . .
- SUMM . . . compounds of Formula (1.0.0) also possess activity as immunosuppressive agents and are especially useful for treating autoimmune diseases in which **inflammation** is a component part of the autoimmune disease, or in which **inflammation** is part of the etiology of the autoimmune disease, or in which **inflammation** is otherwise involved with the autoimmune disease. Alternatively, the compounds of Formula (1.0.0) are anti-inflammatory agents useful in the treatment. . .
- SUMM . . . with the formation of pseudopolyps, i.e., edematous, inflamed islands of mucosa between areas of ulceration; and transmural colitis, which is **inflammation** of the full thickness of the bowel, rather than mucosal and submucosal disease, usually with the formation of noncaseating granulomas, . . .
- SUMM [0497] gout, and fever and pain associated with **inflammation**;
- SUMM [0502] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis; . . .
- SUMM . . . anesthetics for relieving pain, irritation and itching, e.g., benzocaine, lidocaine, dibucaine, and pramoxine hydrochloride; topical analgesics for relieving pain and **inflammation**, e.g., methyl salicylate, camphor, menthol, and resorcinol; topical antiseptics for preventing infection, e.g., benzalkonium chloride and povidone-iodine; and vitamins and. . .
- CLM What is claimed is:
- . . . degenerative arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis;

gout, and fever and pain associated with **inflammation**; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from the . . . conjunctivitis; uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacolytic uveitis; posterior uveitis; disease, disorder, or condition is a member selected from the group consisting of (1) inflammatory diseases and conditions comprising: joint **inflammation**, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .

IT 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfapyrazole 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 64-86-8, Colchicine 76-25-5, Triamcinolone acetate 90-82-4, Pseudoephedrine 101-40-6, Propylhexedrine 113-92-8, Chlorpheniramine 315-30-0, Allopurinol 317-34-0, Aminophylline 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 586-06-1, Orciprenaline 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride 1397-89-3, Amphotericin B 1404-26-8, Polymyxin B 2315-02-8, Oxymetazoline hydrochloride 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromarone 5534-09-8, Beclomethasone dipropionate 7440-57-5D, Gold, derivs. 7683-59-2, Isoprenaline 9004-08-4, Cathepsin 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate 18559-94-9, Salbutamol 22254-24-6, Ipratropium bromide 22916-47-8, Miconazole 23031-25-6, Terbutaline 23593-75-1, Clotrimazole 27220-47-9, Econazole 30392-41-7, Bitolterol mesylate 38677-81-5, Pirbuterol **51333-22-3**, Budesonide **58581-89-8**, Azelastine 59865-13-3, Cyclosporine 65277-42-1, Ketoconazole 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide **79794-75-5**, Loratadine **80474-14-2**, Fluticasone propionate **83799-24-0**, Fexofenadine **83881-51-0**, Cetirizine 83919-23-7, Mometasone furoate 86386-73-4, Fluconazole 89365-50-4, Salmeterol 93211-49-5, L-651392 96566-25-5, Ablukast **100643-71-8**, Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin **107753-78-6**, Zafirlukast **11406-87-2**, Zileuton 118414-82-7, MK-886 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide 128253-31-6, BAY X 1005 140841-32-3, ZD 2138 141579-54-6, Fenleuton 143538-27-6, BAY x 7195 147030-01-1, MK-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast 151581-24-7, Iralukast 154355-76-7, ABT-761 158930-07-5, L-739010 **158966-92-8**, Montelukast 162011-90-7, Rofecoxib 162750-10-9, SB-210661 168154-07-2, L-746530 170277-31-3, Infliximab 185243-69-0, Etanercept 257892-34-5, D 4418 331731-18-1, D 2E7 (in combination with; preparation of biaryl nicotinamides as inhibitors of PDE4 isoenzymes)

L23 ANSWER 6 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2003:265957 USPATFULL

TITLE: Pyrrolyl- and imidazolyl-acid amide derivatives useful as inhibitors of PDE4 isozymes

INVENTOR(S): Marfat, Anthony, UNITED STATES

McKechney, Michael William, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003186974	A1	20031002
	US 6869945	B2	20050322
APPLICATION INFO.:	US 2002-300950	A1	20021120 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2002-62145, filed on 31 Jan 2002, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-265486P	20010131 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	PFIZER INC., PATENT DEPARTMENT, MS8260-1611, EASTERN POINT ROAD, GROTON, CT, 06340	
NUMBER OF CLAIMS:	10	
EXEMPLARY CLAIM:	1	
LINE COUNT:	7140	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		
SUMM	. . . for more selective inhibitors of PDEs that are able to suppress both immune cell functions in vitro and allergic pulmonary inflammation in vivo, while at the same time having improved side-effect profiles. Within the airways of patients suffering from asthma and. . .	
SUMM	[0008] Airflow obstruction and airway inflammation are features of asthma as well as COPD. While bronchial asthma is predominantly characterized by an eosinophilic inflammation , neutrophils appear to play a major role in the pathogenesis of COPD. Thus, PDEs that are involved in smooth muscle. . .	
SUMM	. . . hydrolases from their granules, and the generation of reactive oxygen species, neutrophils contribute to the tissue destruction associated with chronic inflammation , and are further implicated in the pathology of conditions such as emphysema.	
SUMM	. . . 400 mg; Pruniaux et al., "The novel phosphodiesterase inhibitor CI-1018 inhibits antigen-induced lung eosinophilia in sensitized brown-norway rats--comparison with rolipram," Inflammation S-04-6, 1999. CI-1018 has been demonstrated to have good oral bioavailability (57% in the rat) and good oral potency of. . .	
SUMM	[0209] gout, and fever and pain associated with inflammation ;	
SUMM	[0214] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .	
SUMM	. . . In particular, the compounds of Formula (1.0.0) are useful in the treatment of (1) inflammatory diseases and conditions comprising: joint inflammation , rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .	
DETD	. . . (1.0.0) is asthma, a chronic, increasingly common disorder encountered worldwide and characterized by intermittent reversible airway obstruction, airway hyper-responsiveness and inflammation . The cause of asthma has yet to be determined, but the most common pathological expression of asthma is inflammation of the airways, which may be significant even in the airways of patients with	

- mild asthma. Based on bronchial biopsy. . .
- DETD [0435] Pulmonary **Inflammation** in Allergic Cynomolpus Monkeys--The ability of the combinations of therapeutic agents of the present invention to inhibit *Ascaris* antigen induced. . .
- DETD . . . use of primates, is that described in Turner et al., "Characterization of a primate model of asthma using anti-allergy/anti-asthma agents," **Inflammation Research** 45 239-245, 1996.
- DETD [0450] COPD is characterized by **inflammation** of the airways, as is the case with asthma, but the inflammatory cells that have been found in the bronchoalveolar. . .
- DETD . . . a productive cough; staphylococcus or streptococcal bronchitis which are caused by staphylococci or streptococci; and vesicular bronchitis in which the **inflammation** extends into the alveoli, which are sometimes visible under the pleura as whitish-yellow granulations like millet seeds.
- DETD . . . and T-lymphocytes. A variety of inflammatory mediators is also released by these cells, all of which may contribute to the **inflammation** exhibited in the late phase response.
- DETD . . . al "Effect of AWD 12-281, a new selective PDE-4 inhibitor, luteprednol and beclomethasone in models of allergic rhinitis and airway **inflammation** in brown norway-rats," Am. J. Respir. Crit. Care Med. A95, 1999. The compounds D-22888 and AWD-12,281 have already been described. . .
- DETD . . . rhinitis in terms of anatomical proximity as well as a shared etiology and pathogenesis in some cases. Sinusitis is the **inflammation** of a sinus and this condition may be purulent or nonpurulent, as well as acute or chronic. Depending upon the sinus where the **inflammation** is located, the condition is known as ethmoid, frontal, maxillary, or sphenoid sinusitis. The ethmoidal sinus is one type of. . .
- DETD [0472] Arthritis is defined as **inflammation** of the joints, and rheumatoid arthritis is a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammatory. . .
- DETD . . . Accordingly, the term "rheumatoid arthritis" includes acute arthritis, which is arthritis marked by pain, heat, redness, and swelling due to **inflammation**, infection, or trauma; acute gouty arthritis, which is acute arthritis associated with gout; chronic inflammatory arthritis, which is **inflammation** of the joints in chronic disorders such as rheumatoid arthritis; degenerative arthritis, which is osteoarthritis; infectious arthritis, which is arthritis. . . or parasites; Lyme arthritis, which is arthritis of the large joints associated with Lyme 20 disease; proliferative arthritis, which is **inflammation** of the joints with proliferation of the synovium, seen in rheumatoid arthritis; psoriatic arthritis, which is a syndrome in which psoriasis occurs in association with inflammatory arthritis; and vertebral arthritis, which is **inflammation** involving the intervertebral disks.
- DETD [0474] The three major pathological features of rheumatoid arthritis that are responsible for progressive joint destruction are **inflammation**, abnormal cellular and humoral responses, and synovial hyperplasia. The particular cellular pathology of rheumatoid arthritis includes the presence of T-cells. . . disease. Pro-inflammatory cytokines, e.g., IL-1, IL-4, IL-5, IL-6, IL-9, IL-13, and TNF- α , are the major contributors to joint tissue damage, **inflammation**, hyperplasia, pannus formation and bone resorption. See Firestein, G. S. and Zvaifler, W. J., "How important are T-cells in

- chronic rheumatoid. . .
- DETD . . . of the compounds of Formula (1.0.0) to inhibit TNF- α release from stimulated monocytes can be correlated with animal models of **inflammation** in which anti-inflammatory effects can be shown to correspond to suppression of TNF- α accumulation. One such animal model involves inhibition. . .
- DETD . . . are tophi or chalky deposits of sodium urate. Some therapeutic agents are useful in treating both gout and its attendant **inflammation**, e.g., phenylbutazone and colchicine; while other therapeutic agents possess only uricosuric properties, e.g., sulfinpyrazone and benzbromarone
- DETD . . . to the present invention such fever is either that manifested in pharyngoconjunctival fever or rheumatic fever, or that manifested during **inflammation**. A concomitant of **inflammation** is pain, especially that experienced in the joints and connective tissue of those suffering from rheumatoid arthritis and gout.
- DETD . . . PDE4 inhibitory compounds of Formula (1.0.0) provide beneficial results in the treatment of gout, and fever and pain associated with **inflammation**.
- DETD . . . PDE4 inhibitors and their utility in the treatment of rheumatoid arthritis. The activity of rolipram in animal models of acute **inflammation** such as the mouse adjuvant arthritis model, has been demonstrated in the art; Sekut et al, "Anti-inflammatory activity of phosphodiesterase (PDE) IV inhibitors in acute and chronic models of **inflammation**," Olin. Exp. Immunol. 100(1) 126-132, 1995. The ability of rolipram to reduce disease severity in the collagen 11 induced arthritis. . .
- DETD . . . the compound t.i.d. The compound was able to induce a positive trend towards clinical improvement associated with a reduction in **C-reactive protein** and IL-6 serum levels. Chikanza et al, "The clinical effects of RP73401 phosphodiesterase Type 4 inhibitor in patients with rheumatoid. . .
- DETD . . . a central role in the induction of local IgE responses and the recruitment of eosinophils in this disease. The chronic **inflammation** seen in atopic dermatitis is considered to be the result of several interdependent factors, such as repeated or persistent allergen. . . vascular adhesion molecule-1 (VCAM-1), an adhesion molecule involved in the migration of mononuclear cells and eosinophils into sites of tissue **inflammation**. Further, IL-5 is a key mediator of eosinophil activation, which is a common feature of atopic disease.
- DETD . . . conjunctiva is a delicate membrane that lines the eyelids and covers the exposed surface of the sclera. Conjunctivitis is an **inflammation** of the conjunctiva that generally consists of conjunctival hyperemia associated with a discharge. The most common types of conjunctivitis, which. . . which is an acute conjunctivitis caused by bacteria or viruses, particularly gonococci, meningococci, pneumococci, and streptococci, and characterized by severe **inflammation** of the conjunctiva and copious discharge of pus; and vernal conjunctivitis which is a bilateral conjunctivitis of seasonal occurrence, of. . .
- DETD . . . is the vascular middle coat or tunic of the eye, comprising the iris, ciliary body, and choroid. Uveitis is an **inflammation** of all or part of the uvea and commonly involves the other tunics of the eye, i.e., the sclera and. . . the posterior portion, characterized by nodular collections of epithelioid cells and giant cells surrounded by lymphocytes; nongranulomatous uveitis which is **inflammation**

- of the anterior portion of the uveal tract, i.e., the iris and ciliary body; phacoantigenic uveitis which is one of. . .
- DETD . . . number of mediators via either topical or systemic administration. For example, rolipram has been shown to inhibit croton oil-induced ear **inflammation** in the mouse at topical doses as low as 0.03 mg per ear. The selective PDE4 inhibitor Ro 20-1724 has. . .
- DETD [0505] A sclerosis is an induration, or hardening, and refers especially to hardening of a part from **inflammation**, and from increased formation of connective tissue and in diseases of the interstitial substance. The term "sclerosis" is used chiefly. . .
- DETD [0506] Multiple sclerosis is an autoimmune disease that in addition to chronic **inflammation** and demyelination, also results in gliosis within the central nervous system. There are several disease subtypes, including primary progressive multiple. . . subtypes may be distinguished from each other on the basis of the course of the disease, of the type of **inflammation** involved, and through the use of magnetic resonance imaging (MRI). It is also possible for the basic disease mechanism to change during the course of multiple sclerosis, with an **inflammation**-based process being replaced later by one which involves demyelination and axonal damage. See Weillbach and Gold, "Disease modifying treatments for. . .
- DETD . . . compounds of Formula (1.0.0) also possess activity as immunosuppressive agents and are especially useful for treating autoimmune diseases in which **inflammation** is a component part of the autoimmune disease, or in which **inflammation** is part of the etiology of the autoimmune disease, or in which **inflammation** is otherwise involved with the autoimmune disease. Alternatively, the compounds of Formula (1.0.0) are anti-inflammatory agents useful in the treatment. . .
- DETD . . . with the formation of pseudopolyps, i.e., edematous, inflamed islands of mucosa between areas of ulceration; and transmural colitis, which is **inflammation** of the full thickness of the bowel, rather than mucosal and submucosal disease, usually with the formation of noncaseating granulomas,. . .
- DETD [0549] gout, and fever and pain associated with **inflammation**;
- DETD [0554] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis; . . .
- DETD . . . anesthetics for relieving pain, irritation and itching, e.g., benzocaine, lidocaine, dibucaine, and pramoxine hydrochloride; topical analgesics for relieving pain and **inflammation**, e.g., methyl salicylate, camphor, menthol, and resorcinol; topical antiseptics for preventing infection, e.g., benzalkonium chloride and povidone-iodine; and vitamins and. . .
- CLM What is claimed is:
- . . . degenerative arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with **inflammation**; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from the. . . conjunctivitis; uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous

uveitis; phacoantigenic uveitis; posterior uveitis;. . .

IT 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfapyrazone
 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate
 59-42-7, Phenylephrine 64-86-8, Colchicine 76-25-5, Triamcinolone
 acetone 90-82-4, Pseudoephedrine 91-22-5D, Quinoline, derivs.
 101-40-6, Propylhexedrine 113-92-8, Chlorpheniramine 120-72-9D,
 Indole, derivs. 128-39-2D, 2,6-Di-tert-butylphenol, hydrazone derivs.
 315-30-0, Allopurinol 317-34-0, Aminophylline 404-86-4, Capsaicin
 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride
 550-99-2, Naphazoline hydrochloride 581-30-6, 3H-Phenothiazin-3-one
 586-06-1, Orciprenaline 613-46-7D, 2-Cyanonaphthalene, pyridinyl
 derivs. 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride
 1436-43-7, 2-Cyanoquinoline 2315-02-8, Oxymetazoline hydrochloride
 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromarone
 5534-09-8, Beclomethasone dipropionate 6339-87-3D, 2-
 Thiophenesulfonamide, derivs. 7440-57-5D, Gold, aurothio derivs.
 7683-59-2, Isoprenaline 9004-08-4, Cathepsin 10102-43-9, Nitric
 oxide, biological studies 14838-15-4, Phenylpropanolamine 15826-37-6,
 Sodium cromoglycate 18559-94-9, Albuterol 22254-24-6, Ipratropium
 bromide 23031-25-6, Terbutaline 30392-41-7, Bitolterol mesylate
 38677-81-5, Pirbuterol **51333-22-3**, Budesonide
58581-89-8, Azelastine 59865-13-3, Cyclosporine 68844-77-9,
 Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide
 79554-19-1D, derivs. **79794-75-5**, Loratadine **80474-14-2**
 , Fluticasone propionate **83799-24-0**, Fexofenadine 83869-56-1,
 Granulocyte macrophage colony stimulating factor **83881-51-0**,
 Cetirizine 83919-23-7, Mometasone furoate 89365-50-4, Salmeterol
 93211-49-5, L-651392 96566-25-5, Ablukast **100643-71-8**,
 Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin
 106096-93-9, Basic fibroblast growth factor **107753-78-6**,
 Zafirlukast **11406-87-2**, Zileuton 118414-82-7, MK-886
 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide
 128253-31-6, BAY x 1005 128312-51-6 140841-32-3, 2D-2138
 141579-54-6, Fenleuton 141579-87-5 143538-27-6, BAY x 7195
 147030-01-1, MK-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast
 151581-24-7, Iralukast 154355-76-7, ABT-761 158930-07-5, L-739010
158966-92-8, Montelukast 162011-90-7, Rofecoxib 162750-10-9,
 SB-210661 168154-07-2, L-746530 170277-31-3, Infliximab
 185243-69-0, Etanercept 202415-99-4 204974-93-6, BIL 260
 257892-34-5, D 4418 331731-18-1, D 2E7 346735-24-8, BIL 284
 (combination therapy with PDE4 inhibitors; preparation of thiazolyl-,
 oxazolyl-, pyrrolyl-, and imidazolyl- acid amide derivs. as inhibitors
 of PDE4 isoenzymes)

L23 ANSWER 7 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2003:188461 USPATFULL

TITLE: Oxazolyl-acid amide derivatives useful as inhibitors of
 PDE4 isozymes

INVENTOR(S): Marfat, Anthony, UNITED STATES
 McKechney, Michael William, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003130254	A1	20030710
	US 6894041	B2	20050517
APPLICATION INFO.:	US 2002-300959	A1	20021120 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2002-62145, filed on 31 Jan		

2002, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-265486P	20010131 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	PFIZER INC., PATENT DEPARTMENT, MS8260-1611, EASTERN POINT ROAD, GROTON, CT, 06340	
NUMBER OF CLAIMS:	10	
EXEMPLARY CLAIM:	1	
LINE COUNT:	7168	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		
SUMM for more selective inhibitors of PDEs that are able to suppress both immune cell functions in vitro and allergic pulmonary inflammation in vivo, while at the same time having improved side-effect profiles. Within the airways of patients suffering from asthma and. . .	
SUMM	[0008] Airflow obstruction and airway inflammation are features of asthma as well as COPD. While bronchial asthma is predominantly characterized by an eosinophilic inflammation , neutrophils appear to play a major role in the pathogenesis of COPD. Thus, PDEs that are involved in smooth muscle. . .	
SUMM hydrolases from their granules, and the generation of reactive oxygen species, neutrophils contribute to the tissue destruction associated with chronic inflammation , and are further implicated in the pathology of conditions such as emphysema.	
SUMM 400 mg; Pruniaux et al., "The novel phosphodiesterase inhibitor Cl-1018 inhibits antigen-induced lung eosinophilia in sensitized brown-norway rats--comparison with rolipram," Inflammation S-04-6, 1999. Cl-1018 has been demonstrated to have good oral bioavailability (57% in the rat) and good oral potency of. . .	
SUMM	[0221] gout, and fever and pain associated with inflammation ;	
SUMM	[0226] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of inflammation of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .	
SUMM In particular, the compounds of Formula (1.0.0) are useful in the treatment of (1) inflammatory diseases and conditions comprising: joint inflammation , rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .	
DETD (1.0.0) is asthma, a chronic, increasingly common disorder encountered worldwide and characterized by intermittent reversible airway obstruction, airway hyper-responsiveness and inflammation . The cause of asthma has yet to be determined, but the most common pathological expression of asthma is inflammation of the airways, which may be significant even in the airways of patients with mild asthma. Based on bronchial biopsy. . .	
DETD	[0463] Pulmonary Inflammation in Allergic Cynomolques Monkeys--The ability of the combinations of therapeutic agents of the present invention to inhibit Ascaris antigen induced. . .	
DETD use of primates, is that described in Turner et al., "Characterization of a primate model of asthma using anti-allergy/anti-asthma agents," Inflammation Research 45	

239-245, 1996.

- DETD [0478] COPD is characterized by **inflammation** of the airways, as is the case with asthma, but the inflammatory cells that have been found in the bronchoalveolar. . . .
- DETD a productive cough; staphylococcus or streptococcal bronchitis which are caused by staphylococci or streptococci; and vesicular bronchitis in which the **inflammation** extends into the alveoli, which are sometimes visible under the pleura as whitish-yellow granulations like millet seeds.
- DETD and T-lymphocytes. A variety of inflammatory mediators is also released by these cells, all of which may contribute to the **inflammation** exhibited in the late phase response.
- DETD al "Effect of AWD 12-281, a new selective PDE-4 inhibitor, loteprednol and beclomethasone in models of allergic rhinitis and airway **inflammation** in brown norway-rats," Am. J. Respir. Crit. Care Med. A95, 1999. The compounds D-22888 and AWD-12,281 have already been described. . . .
- DETD rhinitis in terms of anatomical proximity as well as a shared etiology and pathogenesis in some cases. Sinusitis is the **inflammation** of a sinus and this condition may be purulent or nonpurulent, as well as acute or chronic. Depending upon the sinus where the **inflammation** is located, the condition is known as ethmoid, frontal, maxillary, or sphenoid sinusitis. The ethmoidal sinus is one type of. . . .
- DETD [0500] Arthritis is defined as **inflammation** of the joints, and rheumatoid arthritis is a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammatory. . . .
- DETD Accordingly, the term "rheumatoid arthritis" includes acute arthritis, which is arthritis marked by pain, heat, redness, and swelling due to **inflammation**, infection, or trauma; acute gouty arthritis, which is acute arthritis associated with gout; chronic inflammatory arthritis, which is **inflammation** of the joints in chronic disorders such as rheumatoid arthritis; degenerative arthritis, which is osteoarthritis; infectious arthritis, which is arthritis. . . . or parasites; Lyme arthritis, which is arthritis of the large joints associated with Lyme 20 disease; proliferative arthritis, which is **inflammation** of the joints with proliferation of the synovium, seen in rheumatoid arthritis; psoriatic arthritis, which is a syndrome in which psoriasis occurs in association with inflammatory arthritis; and vertebral arthritis, which is **inflammation** involving the intervertebral disks.
- DETD [0502] The three major pathological features of rheumatoid arthritis that are responsible for progressive joint destruction are **inflammation**, abnormal cellular and humoral responses, and synovial hyperplasia. The particular cellular pathology of rheumatoid arthritis includes the presence of T-cells. . . . disease. Pro-inflammatory cytokines, e.g., IL-1, IL-4, IL-5, IL-6, IL-9, IL-13, and TNF- α , are the major contributors to joint tissue damage, **inflammation**, hyperplasia, pannus formation and bone resorption. See Firestein, G. S. and Zvaifler, W. J., "How important are T-cells in chronic rheumatoid. . . .
- DETD of the compounds of Formula (1.0.0) to inhibit TNF- α release from stimulated monocytes can be correlated with animal models of **inflammation** in which anti-inflammatory effects can be shown to correspond to suppression of TNF- α accumulation. One such animal model involves inhibition. . . .
- DETD are tophi or chalky deposits of sodium urate. Some therapeutic

agents are useful in treating both gout and its attendant **inflammation**, e.g., phenylbutazone and colchicine; while other therapeutic agents possess only uricosuric properties, e.g., sulfinpyrazone and benzbromarone

DETD . . . to the present invention such fever is either that manifested in pharyngoconjunctival fever or rheumatic fever, or that manifested during **inflammation**. A concomitant of **inflammation** is pain, especially that experienced in the joints and connective tissue of those suffering from rheumatoid arthritis and gout.

DETD . . . PDE4 inhibitory compounds of Formula (1.0.0) provide beneficial results in the treatment of gout, and fever and pain associated with **inflammation**.

DETD . . . PDE4 inhibitors and their utility in the treatment of rheumatoid arthritis. The activity of rolipram in animal models of acute **inflammation** such as the mouse adjuvant arthritis model, has been demonstrated in the art; Sekut et al, "Anti-inflammatory activity of phosphodiesterase (PDE) IV inhibitors in acute and chronic models of **inflammation**," Olin. Exp. Immunol. 100(1) 126-132, 1995. The ability of rolipram to reduce disease severity in the collagen II induced arthritis. . . .

DETD . . . the compound t.i.d. The compound was able to induce a positive trend towards clinical improvement associated with a reduction in **C-reactive protein** and IL-6 serum levels. Chikanza et al, "The clinical effects of RP73401 phosphodiesterase Type 4 inhibitor in patients with rheumatoid. . . .

DETD . . . a central role in the induction of local IgE responses and the recruitment of eosinophils in this disease. The chronic **inflammation** seen in atopic dermatitis is considered to be the result of several interdependent factors, such as repeated or persistent allergen. . . . vascular adhesion molecule-1 (VCAM-1), an adhesion molecule involved in the migration of mononuclear cells and eosinophils into sites of tissue **inflammation**. Further, IL-5 is a key mediator of eosinophil activation, which is a common feature of atopic disease.

DETD . . . conjunctiva is a delicate membrane that lines the eyelids and covers the exposed surface of the sclera. Conjunctivitis is an **inflammation** of the conjunctiva that generally consists of conjunctival hyperemia associated with a discharge. The most common types of conjunctivitis, which. . . . which is an acute conjunctivitis caused by bacteria or viruses, particularly gonococci, meningococci, pneumococci, and streptococci, and characterized by severe **inflammation** of the conjunctiva and copious discharge of pus; and vernal conjunctivitis which is a bilateral conjunctivitis of seasonal occurrence, of. . . .

DETD . . . is the vascular middle coat or tunic of the eye, comprising the iris, ciliary body, and choroid. Uveitis is an **inflammation** of all or part of the uvea and commonly involves the other tunics of the eye, i.e., the sclera and. . . . the posterior portion, characterized by nodular collections of epithelioid cells and giant cells surrounded by lymphocytes; nongranulomatous uveitis which is **inflammation** of the anterior portion of the uveal tract, i.e., the iris and ciliary body; phacoantigenic uveitis which is one of. . . .

DETD . . . number of mediators via either topical or systemic administration. For example, rolipram has been shown to inhibit croton oil-induced ear **inflammation** in the mouse at topical doses as low as 0.03 mg per ear. The selective PDE4 inhibitor Ro 20-1724 has. . . .

- DETD [0533] A sclerosis is an induration, or hardening, and refers especially to hardening of a part from **inflammation**, and from increased formation of connective tissue and in diseases of the interstitial substance. The term "sclerosis" is used chiefly. . .
- DETD [0534] Multiple sclerosis is an autoimmune disease that in addition to chronic **inflammation** and demyelination, also results in gliosis within the central nervous system. There are several disease subtypes, including primary progressive multiple. . . subtypes may be distinguished from each other on the basis of the course of the disease, of the type of **inflammation** involved, and through the use of magnetic resonance imaging (MRI). It is also possible for the basic disease mechanism to change during the course of multiple sclerosis, with an **inflammation**-based process being replaced later by one which involves demyelination and axonal damage. See Weilbach and Gold, "Disease modifying treatments for. . .
- DETD . . . compounds of Formula (1.0.0) also possess activity as immunosuppressive agents and are especially useful for treating autoimmune diseases in which **inflammation** is a component part of the autoimmune disease, or in which **inflammation** is part of the etiology of the autoimmune disease, or in which **inflammation** is otherwise involved with the autoimmune disease. Alternatively, the compounds of Formula (1.0.0) are anti-inflammatory agents useful in the treatment. . .
- DETD . . . with the formation of pseudopolyps, i.e., edematous, inflamed islands of mucosa between areas of ulceration; and transmural colitis, which is **inflammation** of the full thickness of the bowel, rather than mucosal and submucosal disease, usually with the formation of noncaseating granulomas,. . .
- DETD [0577] gout, and fever and pain associated with **inflammation**;
- DETD [0582] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .
- DETD . . . anesthetics for relieving pain, irritation and itching, e.g., benzocaine, lidocaine, dibucaine, and pramoxine hydrochloride; topical analgesics for relieving pain and **inflammation**, e.g., methyl salicylate, camphor, menthol, and resorcinol; topical antiseptics for preventing infection, e.g., benzalkonium chloride and povidone-iodine; and vitamins and. . .
- CLM What is claimed is:
- . . . degenerative arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with **inflammation**; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from the. . . conjunctivitis; uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .
- IT 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfapyrazone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 64-86-8, Colchicine 76-25-5, Triamcinolone acetone 90-82-4, Pseudoephedrine 91-22-5D, Quinoline, derivs. 101-40-6, Propylhexedrine 113-92-8, Chlorpheniramine 120-72-9D, Indole, derivs. 128-39-2D, 2,6-Di-tert-butylphenol, hydrazone derivs.

315-30-0, Allopurinol 317-34-0, Aminophylline 404-86-4, Capsaicin
 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride
 550-99-2, Naphazoline hydrochloride 581-30-6, 3H-Phenothiazin-3-one
 586-06-1, Orciprenaline 613-46-7D, 2-Cyanonaphthalene, pyridinyl
 derivs. 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride
 1436-43-7, 2-Cyanoquinoline 2315-02-8, Oxymetazoline hydrochloride
 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromarone
 5534-09-8, Beclomethasone dipropionate 6339-87-3D, 2-
 Thiophenesulfonamide, derivs. 7440-57-5D, Gold, aurothio derivs.
 7683-59-2, Isoprenaline 9004-08-4, Cathepsin 10102-43-9, Nitric
 oxide, biological studies 14838-15-4, Phenylpropanolamine 15826-37-6,
 Sodium cromoglycate 18559-94-9, Albuterol 22254-24-6, Ipratropium
 bromide 23031-25-6, Terbutaline 30392-41-7, Bitolterol mesylate
 38677-81-5, Pirbuterol **51333-22-3**, Budesonide
58581-89-8, Azelastine 59865-13-3, Cyclosporine 68844-77-9,
 Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide
 79554-19-1D, derivs. **79794-75-5**, Loratadine **80474-14-2**
 , Fluticasone propionate **83799-24-0**, Fexofenadine 83869-56-1,
 Granulocyte macrophage colony stimulating factor **83881-51-0**,
 Cetirizine 83919-23-7, Mometasone furoate 89365-50-4, Salmeterol
 93211-49-5, L-651392 96566-25-5, Ablukast **100643-71-8**,
 Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin
 106096-93-9, Basic fibroblast growth factor **107753-78-6**,
 Zafirlukast **111406-87-2**, Zileuton 118414-82-7, MK-886
 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide
 128253-31-6, BAY x 1005 128312-51-6 140841-32-3, ZD-2138
 141579-54-6, Fenleuton 141579-87-5 143538-27-6, BAY x 7195
 147030-01-1, MK-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast
 151581-24-7, Iralukast 154355-76-7, ABT-761 158930-07-5, L-739010
158966-92-8, Montelukast 162011-90-7, Rofecoxib 162750-10-9,
 SB-210661 168154-07-2, L-746530 170277-31-3, Infliximab
 185243-69-0, Etanercept 202415-99-4 204974-93-6, BIIL 260
 257892-34-5, D 4418 331731-18-1, D 2E7 346735-24-8, BIIL 284
 (combination therapy with PDE4 inhibitors; preparation of thiazolyl-,
 oxazolyl-, pyrrolyl-, and imidazolyl- acid amide derivs. as inhibitors
 of PDE4 isoenzymes)

L23 ANSWER 8 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2003:38198 USPATFULL
 TITLE: Ether derivatives useful as inhibitors of PDE4 isozymes
 INVENTOR(S): Marfat, Anthony, Mystic, CT, UNITED STATES
 Chambers, Robert J., Mystic, CT, UNITED STATES
 Magee, Thomas V., Mystic, CT, UNITED STATES
 PATENT ASSIGNEE(S): Pfizer Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003027845	A1	20030206
	US 6828333	B2	20041207
APPLICATION INFO.:	US 2002-66503	A1	20020131 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-265304P	20010131 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49,	

NEW YORK, NY, 10017-5612

NUMBER OF CLAIMS: 30

EXEMPLARY CLAIM: 1

LINE COUNT: 8073

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . for more selective inhibitors of PDEs that are able to suppress both immune cell functions in vitro and allergic pulmonary **inflammation** in vivo, while at the same time having improved side-effect profiles. Within the airways of patients suffering from asthma and. . .

SUMM [0008] Airflow obstruction and airway **inflammation** are features of asthma as well as COPD. While bronchial asthma is predominantly characterized by an eosinophilic **inflammation**, neutrophils appear to play a major role in the pathogenesis of COPD. Thus, PDEs that are involved in smooth muscle. . .

SUMM . . . hydrolases from their granules, and the generation of reactive oxygen species, neutrophils contribute to the tissue destruction associated with chronic **inflammation**, and are further implicated in the pathology of conditions such as emphysema.

SUMM . . . 400 mg; Pruniaux et al., "The novel phosphodiesterase inhibitor CI-1018 inhibits antigen-induced lung eosinophilia in sensitized brown-norway rats--comparison with rolipram," **Inflammation** 5-04-6, 1999. CI-1018 has been demonstrated to have good oral bioavailability (57% in the rat) and good oral potency of. . .

SUMM [0203] gout, and fever and pain associated with **inflammation**;

SUMM [0208] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cycloitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

SUMM . . . In particular, the compounds of Formula (1.0.0) are useful in the treatment of (1) inflammatory diseases and conditions comprising: joint **inflammation**, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .

SUMM . . . 0) is asthma, a chronic, increasingly common disorder encountered worldwide and characterized by intermittent reversible airway obstruction, airway hyper-responsiveness and **inflammation**. The cause of asthma has yet to be determined, but the most common pathological expression of asthma is **inflammation** of the airways, which may be significant even in the airways of patients with mild asthma. Based on bronchial biopsy. . .

SUMM [0404] Pulmonary **Inflammation** in Allergic Cynomolqus Monkeys

SUMM . . . use of primates, is that described in Turner et al., "Characterization of a primate model of asthma using anti-allergy/anti-asthma agents," **Inflammation** Research 45 239-245, 1996.

SUMM [0421] COPD is characterized by **inflammation** of the airways, as is the case with asthma, but the inflammatory cells that have been found in the bronchoalveolar. . .

SUMM . . . a productive cough; staphylococcus or streptococcal bronchitis which are caused by staphylococci or streptococci; and vesicular bronchitis in which the **inflammation** extends into the alveoli, which are sometimes visible under the pleura as whitish-yellow granulations like millet seeds.

SUMM . . . and T-lymphocytes. A variety of inflammatory mediators is also

- released by these cells, all of which may contribute to the **inflammation** exhibited in the late phase response.
- SUMM . . . al "Effect of AWD 12-281, a new selective PDE-4 inhibitor, loteprednol and beclomethasone in models of allergic rhinitis and airway **inflammation** in brown norway-rats," Am. J. Respir. Crit. Care Med. A95, 1999. The compounds D-22888 and AWD-12,281 have already been described. . . .
- SUMM . . . rhinitis in terms of anatomical proximity as well as a shared etiology and pathogenesis in some cases. Sinusitis is the **inflammation** of a sinus and this condition may be purulent or nonpurulent, as well as acute or chronic. Depending upon the sinus where the **inflammation** is located, the condition is known as ethmoid, frontal, maxillary, or sphenoid sinusitis. The ethmoidal sinus is one type of. . . .
- SUMM [0444] Arthritis is defined as **inflammation** of the joints, and rheumatoid arthritis is a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammatory. . . .
- SUMM . . . Accordingly, the term "rheumatoid arthritis" includes acute arthritis, which is arthritis marked by pain, heat, redness, and swelling due to **inflammation**, infection, or trauma; acute gouty arthritis, which is acute arthritis associated with gout; chronic inflammatory arthritis, which is **inflammation** of the joints in chronic disorders such as rheumatoid arthritis; degenerative arthritis, which is osteoarthritis; infectious arthritis, which is arthritis. . . . or parasites; Lyme arthritis, which is arthritis of the large joints associated with Lyme 20 disease; proliferative arthritis, which is **inflammation** of the joints with proliferation of the synovium, seen in rheumatoid arthritis; psoriatic arthritis, which is a syndrome in which psoriasis occurs in association with inflammatory arthritis; and vertebral arthritis, which is **inflammation** involving the intervertebral disks.
- SUMM [0446] The three major pathological features of rheumatoid arthritis that are responsible for progressive joint destruction are **inflammation**, abnormal cellular and humoral responses, and synovial hyperplasia. The particular cellular pathology of rheumatoid arthritis includes the presence of T-cells. . . . disease. Pro-inflammatory cytokines, e.g., IL-1, IL-4, IL-5, IL-6, IL-9, IL-13, and TNF- α , are the major contributors to joint tissue damage, **inflammation**, hyperplasia, pannus formation and bone resorption. See Firestein, G. S. and Zvaifler, W. J., "How important are T-cells in chronic. . . .
- SUMM . . . of the compounds of Formula (1.0.0) to inhibit TNF- α release from stimulated monocytes can be correlated with animal models of **inflammation** in which anti-inflammatory effects can be shown to correspond to suppression of TNF- α accumulation. One such animal model involves inhibition. . . .
- SUMM . . . are tophi or chalky deposits of sodium urate. Some therapeutic agents are useful in treating both gout and its attendant **inflammation**, e.g., phenylbutazone and colchicine; while other therapeutic agents possess only uricosuric properties, e.g., sulfinpyrazone and benzbromarone. Fever, or pyrexia, may. . . . to the present invention such fever is either that manifested in pharyngoconjunctival fever or rheumatic fever, or that manifested during **inflammation**. A concomitant of **inflammation** is pain, especially that experienced in the joints and connective tissue of those suffering from rheumatoid arthritis and gout.
- SUMM . . . PDE4 inhibitory compounds of Formula (1.0.0) provide beneficial

results in the treatment of gout, and fever and pain associated with **inflammation**.

SUMM PDE4 inhibitors and their utility in the treatment of rheumatoid arthritis. The activity of rolipram in animal models of acute **inflammation** such as the mouse adjuvant arthritis model, has been demonstrated in the art; Sekut et al, "Anti-inflammatory activity of phosphodiesterase (PDE) IV inhibitors in acute and chronic models of **inflammation**," Olin. Exp. Immunol 100(1) 126-132, 1995. The ability of rolipram to reduce disease severity in the collagen II induced arthritis. . . .

SUMM the compound t.i.d. The compound was able to induce a positive trend towards clinical improvement associated with a reduction in **C-reactive protein** and IL-6 serum levels.

SUMM Chikanza et al, "The clinical effects of RP73401 phosphodiesterase Type 4 inhibitor in patients with rheumatoid. . . . a central role in the induction of local IgE responses and the recruitment of eosinophils in this disease. The chronic **inflammation** seen in atopic dermatitis is considered to be the result of several interdependent factors, such as repeated or persistent allergen. . . . vascular adhesion molecule-1 (VCAM-1), an adhesion molecule involved in the migration of mononuclear cells and eosinophils into sites of tissue **inflammation**. Further, IL-5 is a key mediator of eosinophil activation, which is a common feature of atopic disease.

SUMM conjunctiva is a delicate membrane that lines the eyelids and covers the exposed surface of the sclera. Conjunctivitis is an **inflammation** of the conjunctiva that generally consists of conjunctival hyperemia associated with a discharge. The most common types of conjunctivitis, which. . . . which is an acute conjunctivitis caused by bacteria or viruses, particularly gonococci, meningococci, pneumococci, and streptococci, and characterized by severe **inflammation** of the conjunctiva and copious discharge of pus; and vernal conjunctivitis which is a bilateral conjunctivitis of seasonal occurrence, of. . . .

SUMM is the vascular middle coat or tunic of the eye, comprising the iris, ciliary body, and choroid. Uveitis is an **inflammation** of all or part of the uvea and commonly involves the other tunics of the eye, i.e., the sclera and. . . . the posterior portion, characterized by nodular collections of epithelioid cells and giant cells surrounded by lymphocytes; nongranulomatous uveitis which is **inflammation** of the anterior portion of the uveal tract, i.e., the iris and ciliary body; phacoantigenic uveitis which is one of. . . .

SUMM number of mediators via either topical or systemic administration. For example, rolipram has been shown to inhibit croton oil-induced ear **inflammation** in the mouse at topical doses as low as 0.03 mg per ear. The selective PDE4 inhibitor Ro 20-1724 has. . . .

SUMM [0478] A sclerosis is an induration, or hardening, and refers especially to hardening of a part from **inflammation**, and from increased formation of connective tissue and in diseases of the interstitial substance. The term "sclerosis" is used chiefly. . . .

SUMM [0479] Multiple sclerosis is an autoimmune disease that in addition to chronic **inflammation** and demyelination, also results in gliosis within the central nervous system. There are several disease subtypes, including primary progressive multiple. . . . subtypes may be distinguished from each other on the basis of the course of the disease, of the type of **inflammation** involved, and through the use of

magnetic resonance imaging (MRI). It is also possible for the basic disease mechanism to change during the course of multiple sclerosis, with an **inflammation**-based process being replaced later by one which involves demyelination and axonal damage. See Weillbach and Gold, "Disease modifying treatments for. . . .

SUMM . . . compounds of Formula (1.0.0) also possess activity as immunosuppressive agents and are especially useful for treating autoimmune diseases in which **inflammation** is a component part of the autoimmune disease, or in which **inflammation** is part of the etiology of the autoimmune disease, or in which **inflammation** is otherwise involved with the autoimmune disease. Alternatively, the compounds of Formula (1.0.0) are anti-inflammatory agents useful in the treatment. . . .

SUMM . . . with the formation of pseudopolyps, i.e., edematous, inflamed islands of mucosa between areas of ulceration; and transmural colitis, which is **inflammation** of the full thickness of the bowel, rather than mucosal and submucosal disease, usually with the formation of noncaseating granulomas,

SUMM [0522] gout, and fever and pain associated with **inflammation**;

SUMM [0527] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;

SUMM . . . anesthetics for relieving pain, irritation and itching, e.g., benzocaine, lidocaine, dibucaine, and pramoxine hydrochloride; topical analgesics for relieving pain and **inflammation**, e.g., methyl salicylate, camphor, menthol, and resorcinol; topical antiseptics for preventing infection, e.g., benzalkonium chloride and povidone-iodine; and vitamins and. . . .

CLM What is claimed is:

. . . . degenerative arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with **inflammation**; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from the. . . .

. . . conjunctivitis; uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;

. . . disease, disorder, or condition is a member selected from the group consisting of (1) inflammatory diseases and conditions comprising: joint **inflammation**, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . . .

IT 50-24-8, Prednisolone 53-03-2, Prednisone 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfinpyrazone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 64-86-8, Colchicine 76-25-5, Triamcinolone acetonide 90-82-4, Pseudoephedrine 101-40-6, Propylhexedrine 113-92-8, Chlorpheniramine 128-39-2D, 2,6-Di-tert-butylphenol, hydrazone derivs. 315-30-0, Allopurinol 317-34-0, Aminophylline 404-86-4, Capsaicin 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 586-06-1, Metaproterenol 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride 2315-02-8,

Oxymetazoline hydrochloride 3198-07-0 3385-03-3, Flunisolide
 3562-84-3, Benzbromarone 5534-09-8, Beclomethasone dipropionate
 6339-87-3D, Thiophene-2-sulfonamide, derivs. 7440-57-5D, Gold, aurothio
 derivs. 7683-59-2, Isoproterenol 9004-08-4D, Cathepsin, derivs.
 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate
 18559-94-9, Albuterol 22254-24-6, Ipratropium bromide 23031-25-6,
 Terbutaline 28797-61-7, Fipronil 30286-75-0, Oxitropium bromide
 30392-40-6, Bitolterol 38677-81-5, Pirbuterol **51333-22-3**,
 Budesonide **58581-89-8**, Azelastine 59865-13-3, Cyclosporine
 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide
79794-75-5, Loratadine **80474-14-2**, Fluticasone
 propionate 80880-90-6, Telenzepine **83799-24-0**, Fexofenadine
 83869-56-1, Granulocyte-macrophage colony-stimulating factor
83881-51-0, Cetirizine 83919-23-7, Mometasone furoate
 89365-50-4, Salmeterol 93211-49-5, L-651392 96566-25-5, Ablukast
100643-71-8, Desloratadine 103177-37-3, Pranlukast
 103475-41-8, Tepoxalin 106096-93-9, Basic fibroblast growth factor
107753-78-6, Zafirlukast **111406-87-2**, Zileuton
 118414-82-7, MK-886 120128-20-3, RG-12525 120443-16-5, Verlukast
 126544-47-6, Ciclesonide 128253-31-6, BAY x 1005 128312-51-6
 136310-93-5, Tiotropium bromide 140841-32-3 141579-54-6, Fenleuton
 141579-87-5 143538-27-6, BAY x 7195 147030-01-1, MK-591
 147398-01-4, CGS-25019c 147432-77-7, Ontazolast 151581-24-7,
 Iralkast 154355-76-7, ABT-761 158930-07-5, L-739010
158966-92-8, Montelukast 162011-90-7, Rofecoxib 162750-10-9,
 SB-210661 168154-07-2, L-746530 170277-31-3, Infliximab
 171964-73-1, ZD-0892 174636-32-9, Talnetant 185243-69-0, Etanercept
 202415-99-4 204974-93-6, BIIL 260 257892-34-5, D 4418 331731-18-1,
 D 2E7 346735-24-8, BIIL 284 350610-64-9, NKP-608C 446023-33-2, UT
 77

(combination therapy with PDE4 inhibitors; preparation of
 carbamoyl-substituted pyridinyl aryl ether derivs. as inhibitors of
 PDE4 isoenzymes)

L23 ANSWER 9 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2002:338241 USPATFULL

TITLE: Nicotinamide biaryl derivatives useful as inhibitors of
 PDE4 isozymes

INVENTOR(S): Chambers, Robert J., Mystic, CT, UNITED STATES
 Marfat, Anthony, Mystic, CT, UNITED STATES
 Magee, Thomas V., Mystic, CT, UNITED STATES

PATENT ASSIGNEE(S): Pfizer Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002193612	A1	20021219
	US 6649633	B2	20031118
APPLICATION INFO.:	US 2002-62813	A1	20020131 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-265492P	20010131 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49, NEW YORK, NY, 10017-5612	
NUMBER OF CLAIMS:	18	

EXEMPLARY CLAIM: 1
 LINE COUNT: 7001

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . for more selective inhibitors of PDEs that are able to suppress both immune cell functions in vitro and allergic pulmonary **inflammation** in vivo, while at the same time having improved side-effect profiles. Within the airways of patients suffering from asthma and. . .

SUMM [0008] Airflow obstruction and airway **inflammation** are features of asthma as well as COPD. While bronchial asthma is predominantly characterized by an eosinophilic **inflammation**, neutrophils appear to play a major role in the pathogenesis of COPD. Thus, PDEs that are involved in smooth muscle. . .

SUMM . . . hydrolases from their granules, and the generation of reactive oxygen species, neutrophils contribute to the tissue destruction associated with chronic **inflammation**, and are further implicated in the pathology of conditions such as emphysema.

SUMM . . . 400 mg; Pruniaux et al., "The novel phosphodiesterase inhibitor Cl-1018 inhibits antigen-induced lung eosinophilia in sensitized brown-norway rats--comparison with rolipram," **Inflammation** S-04-6, 1999. Cl-1018 has been demonstrated to have good oral bioavailability (57% in the rat) and good oral potency of. . .

SUMM [0192] gout, and fever and pain associated with **inflammation**;

SUMM [0197] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . .

SUMM . . . In particular, the compounds of Formula (1.0.0) are useful in the treatment of (1) inflammatory diseases and conditions comprising: joint **inflammation**, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . .

SUMM . . . (1.0.0) is asthma, a chronic, increasingly common disorder encountered worldwide and characterized by intermittent reversible airway obstruction, airway hyper-responsiveness and **inflammation**. The cause of asthma has yet to be determined, but the most common pathological expression of asthma is **inflammation** of the airways, which may be significant even in the airways of patients with mild asthma. Based on bronchial biopsy. . .

SUMM [0410] Pulmonary **Inflammation** in Allergic Cynomolgus Monkeys--The ability of the combinations of therapeutic agents of the present invention to inhibit Ascaris antigen induced. . .

SUMM . . . use of primates, is that described in Turner et al., "Characterization of a primate model of asthma using anti-allergy/anti-asthma agents," **Inflammation** Research 45 239-245, 1996.

SUMM [0425] COPD is characterized by **inflammation** of the airways, as is the case with asthma, but the inflammatory cells that have been found in the bronchoalveolar. . .

SUMM . . . a productive cough; staphylococcus or streptococcal bronchitis which are caused by staphylococci or streptococci; and vesicular bronchitis in which the **inflammation** extends into the alveoli, which are sometimes visible under the pleura as whitish-yellow granulations like millet seeds.

SUMM . . . and T-lymphocytes. A variety of inflammatory mediators is also

- released by these cells, all of which may contribute to the **inflammation** exhibited in the late phase response.
- SUMM . . . al "Effect of AWD 12-281, a new selective PDE-4 inhibitor, loteprednol and beclomethasone in models of allergic rhinitis and airway **inflammation** in brown norway-rats," Am. J. Respir. Crit. Care Med. A95, 1999. The compounds D-22888 and AWD-12,281 have already been described. . . .
- SUMM . . . rhinitis in terms of anatomical proximity as well as a shared etiology and pathogenesis in some cases. Sinusitis is the **inflammation** of a sinus and this condition may be purulent or nonpurulent, as well as acute or chronic. Depending upon the sinus where the **inflammation** is located, the condition is known as ethmoid, frontal, maxillary, or sphenoid sinusitis. The ethmoidal sinus is one type of. . . .
- SUMM [0447] Arthritis is defined as **inflammation** of the joints, and rheumatoid arthritis is a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammatory. . . .
- SUMM . . . Accordingly, the term "rheumatoid arthritis" includes acute arthritis, which is arthritis marked by pain, heat, redness, and swelling due to **inflammation**, infection, or trauma; acute gouty arthritis, which is acute arthritis associated with gout; chronic inflammatory arthritis, which is **inflammation** of the joints in chronic disorders such as rheumatoid arthritis; degenerative arthritis, which is osteoarthritis; infectious arthritis, which is arthritis. . . . or parasites; Lyme arthritis, which is arthritis of the large joints associated with Lyme 20 disease; proliferative arthritis, which is **inflammation** of the joints with proliferation of the synovium, seen in rheumatoid arthritis; psoriatic arthritis, which is a syndrome in which psoriasis occurs in association with inflammatory arthritis; and vertebral arthritis, which is **inflammation** involving the intervertebral disks.
- SUMM [0449] The three major pathological features of rheumatoid arthritis that are responsible for progressive joint destruction are **inflammation**, abnormal cellular and humoral responses, and synovial hyperplasia. The particular cellular pathology of rheumatoid arthritis includes the presence of T-cells. . . . disease. Pro-inflammatory cytokines, e.g., IL-1, IL-4, IL-5, IL-6, IL-9, IL-13, and TNF- α , are the major contributors to joint tissue damage, **inflammation**, hyperplasia, pannus formation and bone resorption. See Firestein, G. S. and Zvaifler, W. J., "How important are T-cells in chronic. . . .
- SUMM . . . of the compounds of Formula (1.0.0) to inhibit TNF- α release from stimulated monocytes can be correlated with animal models of **inflammation** in which anti-inflammatory effects can be shown to correspond to suppression of TNF- α accumulation. One such animal model involves inhibition. . . .
- SUMM . . . are tophi or chalky deposits of sodium urate. Some therapeutic agents are useful in treating both gout and its attendant **inflammation**, e.g., phenylbutazone and colchicine; while other therapeutic agents possess only uricosuric properties, e.g., sulfinpyrazone and benzbromarone.
- SUMM . . . to the present invention such fever is either that manifested in pharyngoconjunctival fever or rheumatic fever, or that manifested during **inflammation**. A concomitant of **inflammation** is pain, especially that experienced in the joints and connective tissue of those suffering from rheumatoid arthritis and gout.
- SUMM . . . PDE4 inhibitory compounds of Formula (1.0.0) provide beneficial

results in the treatment of gout, and fever and pain associated with **inflammation**.

SUMM PDE4 inhibitors and their utility in the treatment of rheumatoid arthritis. The activity of rolipram in animal models of acute **inflammation** such as the mouse adjuvant arthritis model, has been demonstrated in the art; Sekut et al, "Anti-inflammatory activity of phosphodiesterase (PDE) IV inhibitors in acute and chronic models of **inflammation**," Olin. Exp. Immunol. 100(1) 126-132, 1995. The ability of rolipram to reduce disease severity in the collagen 11 induced arthritis. . . .

SUMM the compound t.i.d. The compound was able to induce a positive trend towards clinical improvement associated with a reduction in **C-reactive protein** and IL-6 serum levels.

SUMM Chikanza et al, "The clinical effects of RP73401 phosphodiesterase Type 4 inhibitor in patients with rheumatoid. . . .
 a central role in the induction of local IgE responses and the recruitment of eosinophils in this disease. The chronic **inflammation** seen in atopic dermatitis is considered to be the result of several interdependent factors, such as repeated or persistent allergen. . . . vascular adhesion molecule-1 (VCAM-1), an adhesion molecule involved in the migration of mononuclear cells and eosinophils into sites of tissue **inflammation**. Further, IL-5 is a key mediator of eosinophil activation, which is a common feature of atopic disease.

SUMM conjunctiva is a delicate membrane that lines the eyelids and covers the exposed surface of the sclera. Conjunctivitis is an **inflammation** of the conjunctiva that generally consists of conjunctival hyperemia associated with a discharge. The most common types of conjunctivitis, which. . . . which is an acute conjunctivitis caused by bacteria or viruses, particularly gonococci, meningococci, pneumococci, and streptococci, and characterized by severe **inflammation** of the conjunctiva and copious discharge of pus; and vernal conjunctivitis which is a bilateral conjunctivitis of seasonal occurrence, of. . . .

SUMM is the vascular middle coat or tunic of the eye, comprising the iris, ciliary body, and choroid. Uveitis is an **inflammation** of all or part of the uvea and commonly involves the other tunics of the eye, i.e., the sclera and. . . . the posterior portion, characterized by nodular collections of epithelioid cells and giant cells surrounded by lymphocytes; nongranulomatous uveitis which is **inflammation** of the anterior portion of the uveal tract, i.e., the iris and ciliary body; phacoantigenic uveitis which is one of. . . .

SUMM number of mediators via either topical or systemic administration. For example, rolipram has been shown to inhibit croton oil-induced ear **inflammation** in the mouse at topical doses as low as 0.03 mg per ear. The selective PDE4 inhibitor Ro 20-1724 has. . . .

SUMM [0480] A sclerosis is an induration, or hardening, and refers especially to hardening of a part from **inflammation**, and from increased formation of connective tissue and in diseases of the interstitial substance. The term "sclerosis" is used chiefly. . . .

SUMM [0481] Multiple sclerosis is an autoimmune disease that in addition to chronic **inflammation** and demyelination, also results in gliosis within the central nervous system. There are several disease subtypes, including primary progressive multiple. . . . subtypes may be distinguished from each other on the basis of the course of the disease, of the type of **inflammation** involved, and through the use of

magnetic resonance imaging (MRI). It is also possible for the basic disease mechanism to change during the course of multiple sclerosis, with an **inflammation**-based process being replaced later by one which involves demyelination and axonal damage. See Weilbach and Gold, "Disease modifying treatments for. . . .

SUMM . . . compounds of Formula (1.0.0) also possess activity as immunosuppressive agents and are especially useful for treating autoimmune diseases in which **inflammation** is a component part of the autoimmune disease, or in which **inflammation** is part of the etiology of the autoimmune disease, or in which **inflammation** is otherwise involved with the autoimmune disease. Alternatively, the compounds of Formula (1.0.0) are anti-inflammatory agents useful in the treatment. . . .

SUMM . . . with the formation of pseudopolyps, i.e., edematous, inflamed islands of mucosa between areas of ulceration; and transmural colitis, which is **inflammation** of the full thickness of the bowel, rather than mucosal and submucosal disease, usually with the formation of noncaseating granulomas,

SUMM [0524] gout, and fever and pain associated with **inflammation**;

SUMM [0529] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;

SUMM . . . anesthetics for relieving pain, irritation and itching, e.g., benzocaine, lidocaine, dibucaine, and pramoxine hydrochloride; topical analgesics for relieving pain and **inflammation**, e.g., methyl salicylate, camphor, menthol, and resorcinol; topical antiseptics for preventing infection, e.g., benzalkonium chloride and povidone-iodine; and vitamins and. . . .

CLM What is claimed is:

. . . . degenerative arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with **inflammation**; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from the. . . .

. . . conjunctivitis; uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;

. . . disease, disorder, or condition is a member selected from the group consisting of (1) inflammatory diseases and conditions comprising: joint **inflammation**, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . . .

IT 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfapyrazone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 64-86-8, Colchicine 76-25-5, Triamcinolone acetone 90-82-4, Pseudoephedrine 101-40-6, Propylhexedrine 132-22-9, Chlorpheniramine 315-30-0, Allopurinol 317-34-0, Aminophylline 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 586-06-1, Orciprenaline 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride 1397-89-3, Amphotericin B 1404-26-8, Polymyxin B 2315-02-8, Oxymetazoline hydrochloride 3198-07-0 3385-03-3,

Flunisolide 3562-84-3, Benzbromarone 5534-09-8, Beclomethasone dipropionate 7440-57-5D, Gold, derivs. 7683-59-2, Isoprenaline 9004-08-4, Cathepsin 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate 18559-94-9, Salbutamol 22254-24-6, Ipratropium bromide 22916-47-8, Miconazole 23031-25-6, Terbutaline 23593-75-1, Clotrimazole 27220-47-9, Econazole 30392-41-7, Bitolterol mesylate 38677-81-5, Pirbuterol **51333-22-3**, Budesonide **58581-89-8**, Azelastine 59865-13-3, Cyclosporine 65277-42-1, Ketoconazole 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide **79794-75-5**, Loratadine **80474-14-2**, Fluticasone propionate **83799-24-0**, Fexofenadine **83881-51-0**, Cetirizine 83919-23-7, Mometasone furoate 86386-73-4, Fluconazole 89365-50-4, Salmeterol 93211-49-5, L-651392 96566-25-5, Ablukast **100643-71-8**, Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin **107753-78-6**, Zafirlukast **111406-87-2**, Zileuton 118414-82-7, MK-886 120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide 128253-31-6, BAY X 1005 140841-32-3, ZD 2138 141579-54-6, Fenleuton 143538-27-6, BAY x 7195 147030-01-1, MK-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast 151581-24-7, Iralukast 154355-76-7, ABT-761 158930-07-5, L-739010 **158966-92-8**, Montelukast 162011-90-7, Rofecoxib 162750-10-9, SB-210661 168154-07-2, L-746530 170277-31-3, Infliximab 185243-69-0, Etanercept 257892-34-5, D 4418 331731-18-1, D 2E7
(in combination with; preparation of biaryl nicotinamides as inhibitors of PDE4 isoenzymes)

L23 ANSWER 10 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2002:228358 USPATFULL

TITLE: Thiazolyl-, oxazolyl-, pyrrolyl-, and imidazolyl-acid amide derivatives useful as inhibitors of PDE4 isozymes

INVENTOR(S): Marfat, Anthony, Mystic, CT, UNITED STATES

PATENT ASSIGNEE(S): McKechney, Michael William, Fairport, NY, UNITED STATES
Pfizer Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002123520	A1	20020905
	US 6559168	B2	20030506
APPLICATION INFO.:	US 2002-62145	A1	20020131 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-265486P	20010131 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49, NEW YORK, NY, 10017-5612	
NUMBER OF CLAIMS:	10	
EXEMPLARY CLAIM:	1	
LINE COUNT:	6963	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		
SUMM	. . . for more selective inhibitors of PDEs that are able to suppress both immune cell functions in vitro and allergic pulmonary inflammation in vivo, while at the same time having improved side-effect profiles. Within the airways of patients suffering from asthma and. . .	

- SUMM [0008] Airflow obstruction and airway **inflammation** are features of asthma as well as COPD. While bronchial asthma is predominantly characterized by an eosinophilic **inflammation**, neutrophils appear to play a major role in the pathogenesis of COPD. Thus, PDEs that are involved in smooth muscle. . . .
- SUMM hydrolases from their granules, and the generation of reactive oxygen species, neutrophils contribute to the tissue destruction associated with chronic **inflammation**, and are further implicated in the pathology of conditions such as emphysema.
- SUMM 400 mg; Pruniaux et al., "The novel phosphodiesterase inhibitor CI-1018 inhibits antigen-induced lung eosinophilia in sensitized brown-norway rats--comparison with rolipram," **Inflammation** S-04-6, 1999. CI-1018 has been demonstrated to have good oral bioavailability (57% in the rat) and good oral potency of. . . .
- SUMM [0208] gout, and fever and pain associated with **inflammation**;
- SUMM [0213] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis;. . . .
- SUMM In particular, the compounds of Formula (1.0.0) are useful in the treatment of (1) inflammatory diseases and conditions comprising: joint **inflammation**, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, inflammatory bowel disease, ulcerative colitis, chronic glomerulonephritis, dermatitis, and Crohn's disease; (2) respiratory diseases and. . . .
- SUMM (1.0.0) is asthma, a chronic, increasingly common disorder encountered worldwide and characterized by intermittent reversible airway obstruction, airway hyper-responsiveness and **inflammation**. The cause of asthma has yet to be determined, but the most common pathological expression of asthma is **inflammation** of the airways, which may be significant even in the airways of patients with mild asthma. Based on bronchial biopsy. . . .
- SUMM [0435] Pulmonary **Inflammation** in Allergic Cynomolgus Monkeys
- SUMM use of primates, is that described in Turner et al., "Characterization of a primate model of asthma using anti-allergy/anti-asthma agents," **Inflammation Research** 45 239-245, 1996.
- SUMM [0452] COPD is characterized by **inflammation** of the airways, as is the case with asthma, but the inflammatory cells that have been found in the bronchoalveolar. . . .
- SUMM a productive cough; staphylococcus or streptococcal bronchitis which are caused by staphylococci or streptococci; and vesicular bronchitis in which the **inflammation** extends into the alveoli, which are sometimes visible under the pleura as whitish-yellow granulations like millet seeds.
- SUMM and T-lymphocytes. A variety of inflammatory mediators is also released by these cells, all of which may contribute to the **inflammation** exhibited in the late phase response.
- SUMM al "Effect of AWD 12-281, a new selective PDE-4 inhibitor, luteprednol and beclomethasone in models of allergic rhinitis and airway **inflammation** in brown norway-rats," Am. J. Respir. Crit. Care Med. A95, 1999. The compounds D-22888 and AWD-12,281 have already been described. . . .
- SUMM rhinitis in terms of anatomical proximity as well as a shared etiology and pathogenesis in some cases. Sinusitis is the **inflammation** of a sinus and this condition may be purulent or

nonpurulent, as well as acute or chronic. Depending upon the sinus where the **inflammation** is located, the condition is known as ethmoid, frontal, maxillary, or sphenoid sinusitis. The ethmoidal sinus is one type of. . .

- SUMM [0475] Arthritis is defined as **inflammation** of the joints, and rheumatoid arthritis is a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammation. . .
- SUMM . . . Accordingly, the term "rheumatoid arthritis" includes acute arthritis, which is arthritis marked by pain, heat, redness, and swelling due to **inflammation**, infection, or trauma; acute gouty arthritis, which is acute arthritis associated with gout; chronic inflammatory arthritis, which is **inflammation** of the joints in chronic disorders such as rheumatoid arthritis; degenerative arthritis, which is osteoarthritis; infectious arthritis, which is arthritis. . . or parasites; Lyme arthritis, which is arthritis of the large joints associated with Lyme 20 disease; proliferative arthritis, which is **inflammation** of the joints with proliferation of the synovium, seen in rheumatoid arthritis; psoriatic arthritis, which is a syndrome in which psoriasis occurs in association with inflammatory arthritis; and vertebral arthritis, which is **inflammation** involving the intervertebral disks.
- SUMM [0477] The three major pathological features of rheumatoid arthritis that are responsible for progressive joint destruction are **inflammation**, abnormal cellular and humoral responses, and synovial hyperplasia. The particular cellular pathology of rheumatoid arthritis includes the presence of T-cells. . . disease. Pro-inflammatory cytokines, e.g., IL-1, IL-4, IL-5, IL-6, IL-9, IL-13, and TNF- α , are the major contributors to joint tissue damage, **inflammation**, hyperplasia, pannus formation and bone resorption. See Firestein, G. S. and Zvaifler, W. J., "How important are T-cells in chronic rheumatoid. . .
- SUMM . . . of the compounds of Formula (1.0.0) to inhibit TNF- α release from stimulated monocytes can be correlated with animal models of **inflammation** in which anti-inflammatory effects can be shown to correspond to suppression of TNF- α accumulation. One such animal model involves inhibition. . .
- SUMM . . . are tophi or chalky deposits of sodium urate. Some therapeutic agents are useful in treating both gout and its attendant **inflammation**, e.g., phenylbutazone and colchicine; while other therapeutic agents possess only uricosuric properties, e.g., sulfinpyrazone and benzbromarone.
- SUMM . . . to the present invention such fever is either that manifested in pharyngoconjunctival fever or rheumatic fever, or that manifested during **inflammation**. A concomitant of **inflammation** is pain, especially that experienced in the joints and connective tissue of those suffering from rheumatoid arthritis and gout.
- SUMM . . . PDE4 inhibitory compounds of Formula (1.0.0) provide beneficial results in the treatment of gout, and fever and pain associated with **inflammation**.
- SUMM . . . PDE4 inhibitors and their utility in the treatment of rheumatoid arthritis. The activity of rolipram in animal models of acute **inflammation** such as the mouse adjuvant arthritis model, has been demonstrated in the art; Sekut et al, "Anti-inflammatory activity of phosphodiesterase (PDE) IV inhibitors in acute and chronic models of **inflammation**," Olin. Exp. Immunol. 100(1) 126-132, 1995. The ability of rolipram to reduce disease severity in the collagen 11 induced arthritis. . .

- SUMM . . . the compound t.i.d. The compound was able to induce a positive trend towards clinical improvement associated with a reduction in **C-reactive protein** and IL-6 serum levels. Chikanza et al, "The clinical effects of RP73401 phosphodiesterase Type 4 inhibitor in patients with rheumatoid. . .
- SUMM . . . a central role in the induction of local IgE responses and the recruitment of eosinophils in this disease. The chronic **inflammation** seen in atopic dermatitis is considered to be the result of several interdependent factors, such as repeated or persistent allergen. . . vascular adhesion molecule-1 (VCAM-1), an adhesion molecule involved in the migration of mononuclear cells and eosinophils into sites of tissue **inflammation**. Further, IL-5 is a key mediator of eosinophil activation, which is a common feature of atopic disease.
- SUMM . . . conjunctiva is a delicate membrane that lines the eyelids and covers the exposed surface of the sclera. Conjunctivitis is an **inflammation** of the conjunctiva that generally consists of conjunctival hyperemia associated with a discharge. The most common types of conjunctivitis, which. . . which is an acute conjunctivitis caused by bacteria or viruses, particularly gonococci, meningococci, pneumococci, and streptococci, and characterized by severe **inflammation** of the conjunctiva and copious discharge of pus; and vernal conjunctivitis which is a bilateral conjunctivitis of seasonal occurrence, of. . .
- SUMM . . . is the vascular middle coat or tunic of the eye, comprising the iris, ciliary body, and choroid. Uveitis is an **inflammation** of all or part of the uvea and commonly involves the other tunics of the eye, i.e., the sclera and. . . the posterior portion, characterized by nodular collections of epithelioid cells and giant cells surrounded by lymphocytes; nongranulomatous uveitis which is **inflammation** of the anterior portion of the uveal tract, i.e., the iris and ciliary body; phacoantigenic uveitis which is one of. . .
- SUMM . . . number of mediators via either topical or systemic administration. For example, rolipram has been shown to inhibit croton oil-induced ear **inflammation** in the mouse at topical doses as low as 0.03 mg per ear. The selective PDE4 inhibitor Ro 20-1724 has. . .
- SUMM [0510] A sclerosis is an induration, or hardening, and refers especially to hardening of a part from **inflammation**, and from increased formation of connective tissue and in diseases of the interstitial substance. The term "sclerosis" is used chiefly. . .
- SUMM [0511] Multiple sclerosis is an autoimmune disease that in addition to chronic **inflammation** and demyelination, also results in gliosis within the central nervous system. There are several disease subtypes, including primary progressive multiple. . . subtypes may be distinguished from each other on the basis of the course of the disease, of the type of **inflammation** involved, and through the use of magnetic resonance imaging (MRI). It is also possible for the basic disease mechanism to change during the course of multiple sclerosis, with an **inflammation**-based process being replaced later by one which involves demyelination and axonal damage. See Weilbach and Gold, "Disease modifying treatments for. . .
- SUMM . . . compounds of Formula (1.0.0) also possess activity as immunosuppressive agents and are especially useful for treating autoimmune diseases in which **inflammation** is a component part of the autoimmune disease, or in which **inflammation** is part of the etiology of the autoimmune disease, or in which **inflammation**

is otherwise involved with the autoimmune disease. Alternatively, the compounds of Formula (1.0.0) are anti-inflammatory agents useful in the treatment. . . .

SUMM . . . with the formation of pseudopolyps, i.e., edematous, inflamed islands of mucosa between areas of ulceration; and transmural colitis, which is **inflammation** of the full thickness of the bowel, rather than mucosal and submucosal disease, usually with the formation of noncaseating granulomas, . . .

SUMM [0554] gout, and fever and pain associated with **inflammation**;

SUMM [0559] uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis; . . .

SUMM . . . anesthetics for relieving pain, irritation and itching, e.g., benzocaine, lidocaine, dibucaine, and pramoxine hydrochloride; topical analgesics for relieving pain and **inflammation**, e.g., methyl salicylate, camphor, menthol, and resorcinol; topical antiseptics for preventing infection, e.g., benzalkonium chloride and povidone-iodine; and vitamins and. . .

CLM What is claimed is:

. . . degenerative arthritis; infectious arthritis; Lyme arthritis; proliferative arthritis; psoriatic arthritis; and vertebral arthritis; gout, and fever and pain associated with **inflammation**; an eosinophil-related disorder of whatever type, etiology, or pathogenesis; or an eosinophil-related disorder that is a member selected from the . . . conjunctivitis; uveitis of whatever type, etiology, or pathogenesis; or uveitis that is a member selected from the group consisting of **inflammation** of all or part of the uvea; anterior uveitis; iritis; cyclitis; iridocyclitis; granulomatous uveitis; nongranulomatous uveitis; phacoantigenic uveitis; posterior uveitis; . . .

IT 57-22-7, Vincristine 57-66-9, Probenecid 57-96-5, Sulfinpyrazone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-42-7, Phenylephrine 64-86-8, Colchicine 76-25-5, Triamcinolone acetone 90-82-4, Pseudoephedrine 91-22-5D, Quinoline, derivs. 101-40-6, Propylhexedrine 120-72-9D, Indole, derivs. 128-39-2D, 2,6-Di-tert-butylphenol, hydrazine derivs. 132-22-9, Chlorpheniramine 315-30-0, Allopurinol 317-34-0, Aminophylline 404-86-4, Capsaicin 446-86-6, Azathioprine 522-48-5, Tetrahydrozoline hydrochloride 550-99-2, Naphazoline hydrochloride 581-30-6, 3H-Phenothiazine-3-one 586-06-1, Orciprenaline 613-46-7D, 2-Cyanonaphthalene, pyridinyl derivs. 865-21-4, Vinblastine 1218-35-5, Xylometazoline hydrochloride 1436-43-7, 2-Cyanoquinoline 2315-02-8, Oxymetazoline hydrochloride 3198-07-0 3385-03-3, Flunisolide 3562-84-3, Benzbromarone 5534-09-8, Beclomethasone dipropionate 6339-87-3D, 2-Thiophenesulfonamide, derivs. 7440-57-5D, Gold, aurothio derivs. 7683-59-2, Isoprenaline 9004-08-4, Cathepsin 10102-43-9, Nitric oxide, biological studies 14838-15-4, Phenylpropanolamine 15826-37-6, Sodium cromoglycate 18559-94-9, Albuterol 22254-24-6, Ipratropium bromide 23031-25-6, Terbutaline 30392-41-7, Bitolterol mesylate 38677-81-5, Pirbuterol 51333-22-3, Budesonide 58581-89-8, Azelastine 59865-13-3, Cyclosporine 68844-77-9, Astemizole 73573-87-2, Formoterol 75706-12-6, Leflunomide 79554-19-1D, derivs. 79794-75-5, Loratadine 80474-14-2, Fluticasone propionate 83799-24-0, Fexofenadine 83869-56-1, Granulocyte macrophage colony stimulating factor 83881-51-0, Cetirizine 83919-23-7, Mometasone furoate 89365-50-4, Salmeterol

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93211-49-5, L-651392 96566-25-5, Ablukast **100643-71-8**,
Desloratadine 103177-37-3, Pranlukast 103475-41-8, Tepoxalin
106096-93-9, Basic fibroblast growth factor **107753-78-6**,
Zafirlukast **111406-87-2**, Zileuton 118414-82-7, MK-886
120128-20-3, RG-12525 120443-16-5, Verlukast 126544-47-6, Ciclesonide
128253-31-6, BAY x 1005 128312-51-6 140841-32-3, ZD-2138
141579-54-6, Fenleuton 141579-87-5 143538-27-6, BAY x 7195
147030-01-1, MK-591 147398-01-4, CGS-25019c 147432-77-7, Ontazolast
151581-24-7, Iralukast 154355-76-7, ABT-761 158930-07-5, L-739010
158966-92-8, Montelukast 162011-90-7, Rofecoxib 162750-10-9,
SB-210661 168154-07-2, L-746530 170277-31-3, Infliximab
185243-69-0, Etanercept 202415-99-4 204974-93-6, BIIL 260
257892-34-5, D 4418 331731-18-1, D 2E7 346735-24-8, BIIL 284
(combination therapy with PDE4 inhibitors; preparation of thiazolyl-,
oxazolyl-, pyrrolyl-, and imidazolyl- acid amide derivs. as inhibitors
of PDE4 isoenzymes)

=> FIL STNGUIDE
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION

FULL ESTIMATED COST

133.56	235.69
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION

CA SUBSCRIBER PRICE

-1.60	-1.60
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FILE 'STNGUIDE' ENTERED AT 09:29:17 ON 03 MAR 2008
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb 29, 2008 (20080229/UP).

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION

FULL ESTIMATED COST

1.32	237.01
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION

CA SUBSCRIBER PRICE

0.00	-1.60
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STN INTERNATIONAL LOGOFF AT 09:42:27 ON 03 MAR 2008

Jagoe